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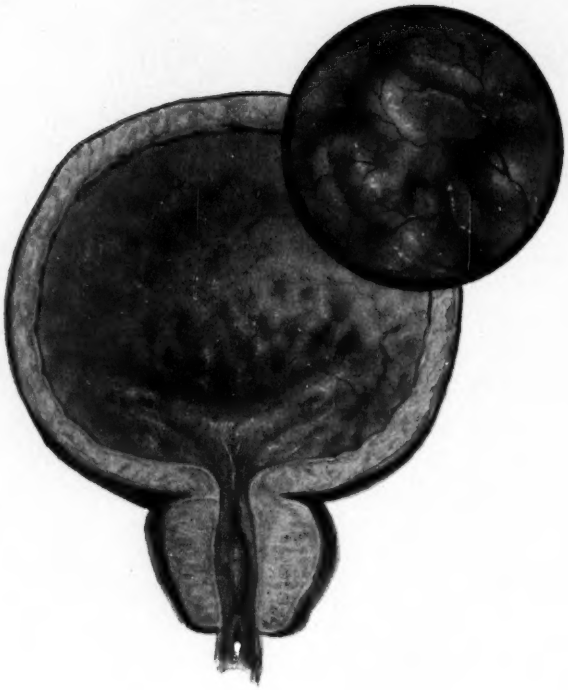

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Douglas, R. G.; Ball, T. L., and Davis, I. F.: California Med. 73:463 (Dec.) 1950.

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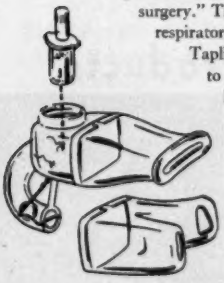

Taplin et al.[1] state that nearly all organisms infecting the respiratory tract are sensitive to either penicillin or streptomycin and that these drugs in micronized form for inhalation appear to offer definite advantages over other methods of administration. Further, "that prophylactic measures used to prevent the accumulation of bronchial secretions have materially reduced the incidence" of postoperative pneumonia. Against penicillin-susceptible organisms, the AEROHALOR plays an important role. The treatment is simple and effective—the patient simply "smokes" the AEROHALOR like a pipe. For comprehensive literature which discusses indications, dosage and clinical results, write Abbott Laboratories, North Chicago, Illinois.

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1. Taplin, G., Cohen, S., and Mahoney, E. (1948), Prevention of Postoperative Pulmonary Infections, J. Amer. Med. Assn., 138:4, Sept. 4.

2. Krasno, L., and Rhoads, P. (1949), The Inhalation of Penicillin Dust; Its Proper Role in the Management of Respiratory Infections, Amer. Prac., 11:649, July.

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VOLUME 63 JULY 1951 NUMBER 1

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Editorials

NEW EDITORIAL SECTION

Dr. Joseph Garland, editor of the *New England Journal of Medicine*, in an article on "Editorials and Medical Journalism" (*World M. A. Bull.* 3: 8-14 [Jan.] 1951) quotes from the second edition of "Webster's New Internationl Dictionary," published in 1949. In this dictionary an editorial is defined as "a leading article in a newspaper or magazine; an editorial article; an article published as an expression of the views of the editor or those of the person or persons in control of the paper." In his most interesting paper, Garland outlines the background of modern medical journalism. In commenting on medical editorials he divides them into (1) scientific editorials, which "may refer to a specific published article, emphasizing its highlights, or it may summarize the existing knowledge of some new development in the field of medicine," and (2) all others "that seek to clear some of the perplexing problems. . . . but it should have always some catalytic function and contain some philosophy in the sense of 'practical or moral wisdom'."

Continuing, Garland says: "The general purpose of the editorial is to direct the readers' attention to a subject and to stimulate his thought upon it. Frequently, but less often, it may express the opinion on that subject of the editor, the editorial board . . . and attempt to guide the thought of the reader according to such opinion."

These ideas and principles appeal to the Chief Editor of the A. M. A. ARCHIVES OF SURGERY, and with the assistance of the other members of the editorial board, an Editorial Section will be developed. Invitations will be sent to members of the medical and surgical profession to submit editorials for publication, which may be signed or unsigned according to the desire of the writers and the editors.

Dr. Lester Dragstedt, a member of the Editorial Board, will assume the major responsibility for the Editorial Section and the Chief Editor will lend a hand as indicated. Dr. Dragstedt has much to contribute to the project, and his selection is in keeping with the established policy of drawing on the talents and abilities of all the members of the Editorial Board. Thus Dr. G. E. Lindskog oversees the section "Surgical Clinics," Dr. Robert Elman, the "Surgical Forum" and Dr. Frank Hinman Jr., the "Case Reports."

These and the other members of the Editorial Board, Drs. Arthur W. Allen, Alfred Blalock, Alton Ochsner, Barnes Woodhall, and the Chief Editor review articles submitted for publication and read widely in other journals.

WALTMAN WALTERS, M.D.
Chief Editor.

LIMITATIONS OF SURGERY IN THE TREATMENT OF MALIGNANT DISEASES

THE PRESENT situation in regard to the treatment of malignancy is far from satisfactory. Our resources consist chiefly of surgical removal and exposure to radiant energy in various forms. Neither of these methods is always applicable, and certainly neither is always successful. In fact, one of the greatest problems confronting medical science is the discovery of a better attack on malignant disease. The inadequacy of current surgical procedures in many cases has stimulated efforts to secure better results by an extension of the magnitude and compass of the operative attack. Such extension has become more feasible with the development of supportive and rehabilitative measures such as improved understanding of blood chemistry, the free use of whole blood transfusions, and the increased safety of prolonged anesthesia. This combination of a desire for better results and the possibility of executing more radical attacks has resulted in the accomplishment of drastic destructive operations that would have been held impossible a few years ago.

In appraising the value of such procedures there are a number of factors that must be considered. Obviously the immediate mortality is of major significance. In the earlier efforts at expanded operation, the hospital mortality was forbidding. This has improved somewhat with added experience. But it is no answer to the increased hazard of such operations to say that these patients would die anyhow. Any therapeutic measure that, of itself, causes a high percentage of deaths in the effort to ward off later death from disease, is of necessity of doubtful validity. To say that the surgeon has no right to withhold extremely radical operations in advanced cases of malignant disease because a few might thus have their period of survival somewhat prolonged is to overlook the responsibility incurred in ending abruptly or greatly shortening the survival period of a far greater number of patients subjected to such operations.

The matter of postoperative morbidity is also of great importance. After many of these extremely radical operations, the survivors suffer grave loss of function, intolerable distress and discomfort, extensive mutilation and disfigurement, loss of weight and strength that are most difficult to correct. These conditions may persist for long periods or for the balance of the patient's life. It is of little consolation to point out to the patient that some of his preoperative complaints have disappeared. One needs to be either optimistic or cynical to be able to say "After all, the human residue is happier by the exchange of discomforts." There is a valuable and legitimate place for the use of avowedly palliative surgery in the treatment of incurable malignant disease, but obviously these extensively destructive operations designed in the hope of definitive cure cannot be secondarily defended as palliative. In most cases the result is actually just the opposite.

Apart from the highly practical objections based on mortality and morbidity, there are fundamental weaknesses in the underlying philosophy of these ultraradical operations for malignant disease. The surgical principle involved in attack on cancer may be stated simply as the removal of the primary disease itself, and all the tissues in continuity with it to the farthest limit of its spread, consistent with survival of the patient and the preservation of a reasonably tolerable state of health and comfort after recovery. An example of the application of this principle is the Halsted operation

for cancer of the breast. Pathology and clinical experience alike have made it clear that the growing microscopic frontier of the disease is apt to be much beyond the farthest obvious and palpable evidence of spread. Hence there have been developed in the field of breast cancer certain generally accepted clinical findings that indicate the hopelessness of efforts to eradicate the disease because it has already transgressed the limits of curability. It is just here that the newer attacks on malignant disease have introduced a new approach. Perhaps not clearly recognized by its own proponents, the idea now seems to be to expand the field of excision to the absolute limits of viability, without much regard for the probable limits of extension of the disease. Thus the gross evidence of the spread of the lesion may lead the enthusiast to remove the entire stomach, the spleen, the pancreas, the transverse colon, and the left lobe of the liver. But what real likelihood is there that the invisible periphery of growth has been successfully encompassed, if the gross disease has made all these organs seem unsafe to leave in place? It is this fact of the indeterminate extent of malignant disease that causes its surgical treatment to lack the sharp definition of many other surgical fields. An inflamed appendix presents a clear-cut indication for removal. A perforated ulcer needs to be closed. A hernia needs to be repaired. A congenital anomaly requires mechanical correction. In all these instances the problem has a definite objective or end point. There is no such anatomical or functional terminus to the spread of cancer and hence to the extent of its operative attack. One is forced to say that the extent of the operation is dependent upon a proper balancing of two objectives—to try to excise the area of invasion, and to preserve the life of the patient and his subsequent well-being. If the disease is so extensive that its complete removal is improbable, there is very little salvage in even the most radical operation. If the operation is so destructive that the patient dies or becomes a surgical invalid there is little justification in the chance that perhaps all the disease has been removed. In short, as has been said elsewhere, the situation is similar to those in which the economists describe the law of so-called diminishing returns. By this they mean that in many economic and productive enterprises there comes a point at which the cost of increasing production more than offsets the profits to be derived from it. Similarly, in the surgery of cancer there comes a point where the effort to combat the disease by further expanding the scope of destructive or ablative operations carries with it great penalties that outweigh the slender benefits to be expected. Each surgeon must decide for himself where this point lies. Nothing that has been said should be used as an excuse for undue hesitancy in attacking boldly even difficult situations where there is a reasonable prospect of a successful outcome for that particular patient. But, on the other hand, the mere fact that it is possible in some instances for people to recover from surprisingly extensive surgical mutilations does not make it wise or desirable to perform such operations. Most of all is it inexcusable to try to emulate someone else's exploits in this field, merely as a demonstration of craftsmanship or a response to challenge. We can all think and work, or at least hope, for a better, more fundamental method of attack on the problem of malignant disease. But at this present time the practicing surgeon should remember that when he is dealing with a patient suffering with malignant disease he is not treating abstract cancer. He is treating an ill individual and his concern should be to do the thing that will best help that particular person.

HARVEY B. STONE, M.D.

SPERMATOGENIC REBOUND IN THE HUMAN FOLLOWING THE ADMINISTRATION OF TESTOSTERONE PROPIONATE

NORRIS J. HECKEL, M.D.
CHICAGO

IN A STUDY on the effect of male sex hormones on benign prostatic hypertrophy in man, I also reported in 1939 the effect of this hormone on the human testis.[1] These observations showed that a man would become temporarily azoospermic or sterile after the administration of this hormone. It was also noted in one man who was followed for a period of time after he became azoospermic that the number of spermatozoa far exceeded pretreatment numbers. This phenomena created a great deal of interest and curiosity, and as a result further observations have been made. Recently Heller and others [2] reported the result of their testicular biopsy studies from androgenically normal men who were given testosterone propionate. In their studies they obtained testicular biopsies before the administration of this hormone, at the end of treatment and six to 17 months after treatment. They discovered that after the administration of a course of testosterone propionate there was a complete disappearance of Leydig cells, marked decrease in the size of the seminiferous tubules, arrest of spermatogenesis with necrosis of the germinal elements and hyalinization and sclerosis of the basement membrane and tunica propria of the tubules. Biopsies taken six months and 17 months after cessation of treatment showed not only recovery from the temporary damage but that the testicular morphology was improved over the pretreatment status if originally the testis was less than excellent.

Rosso, Kestel and I [3] have recently reported our observations of the effect of testosterone propionate in five sterility patients who had a moderate oligospermia of undetermined etiology.

In each one of the five patients who were made azoospermic, or nearly so, there was a striking increase in the number of spermatozoa which far exceeded pretreatment numbers.

Since then our observations have been extended to an additional group of 44 men. They all had barren marriages and were carefully selected and screened from a large group whose common denominator was sterility. In general these men were healthy, normal persons. They were in the second to the fourth decade of life.

From the Department of Urology (Rush) of the University of Illinois College of Medicine.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Nov. 29, 1950.

1. Heckel, N. J.: Influence of Testosterone Propionate upon Benign Prostatic Hypertrophy and Spermatogenesis: A Clinical and Pathological Study. J. Urol. **43**:286, 1940.

2. Heller, C. G.; Nelson, W. O.; Hill, I. C.; Henderson, E.; Maddock, W. O., and Jungck, E. C.: The Effect of Testosterone Administration upon the Human Testis, J. Clin. Endocrinol. **10**:816, 1950.

3. Heckel, N. J.; Rosso, W. A., and Kestel, L. M. T.: Spermatogenic Rebound Phenomena After Administration of Testosterone Propionate, J. Clin. Endocrinol., to be published.

They appeared to be in excellent nutritional state. This group presented no evidence of any obvious endocrine disturbance. Their weights and heights were within normal limits for their age. The physical examination and various laboratory studies, including basal metabolism tests, showed no unusual findings. All were oligospermic, with the total spermatozoa count of the group varying from around 5,000,000 up to 60,000,000. No cause could be discovered for their oligospermia. In each case a testicular biopsy was done before treatment was started. The histological picture of the biopsy material was in general about the same (figs. 1 and 2), namely, a

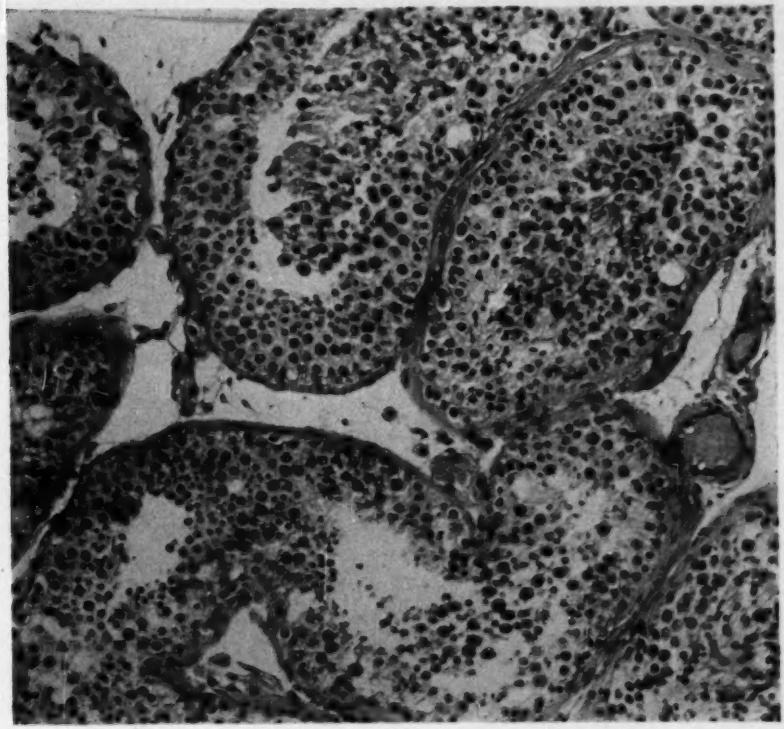

Fig. 1 (M. T., aged 43).—Testicular biopsy before treatment. Total sperm count was 50,000,000. There are focal areas of hypospermatogenesis. Some thickening of the basement membrane is seen.

disruption and disintegration of the normal pattern of sperm development. This occurred at various levels, in some instances at the level of the primary and secondary spermatocytes and in others at the level of the spermatogenic cells. In not a few the basement membrane was thickened. The interstitial structure in the majority appeared to be within normal limits. From the histological picture it seemed that the changes in the mechanism of sperm development as interpreted from the biopsies were not severe enough to be irreversible.

Therefore, this group of men were made azoospermic, or nearly so, by the intramuscular administration of 150 mg. of testosterone propionate per week in a dose of 50 mg. When the total sperm counts approached azoospermic levels, treatment was stopped and an analysis made of the seminal fluid at six to eight week intervals; also testicular biopsies were done on some of the patients at what we considered to be the height of the rebound phase of the sperm count. At this time enough evidence has been collected from 18 of this group of patients to make the following statements

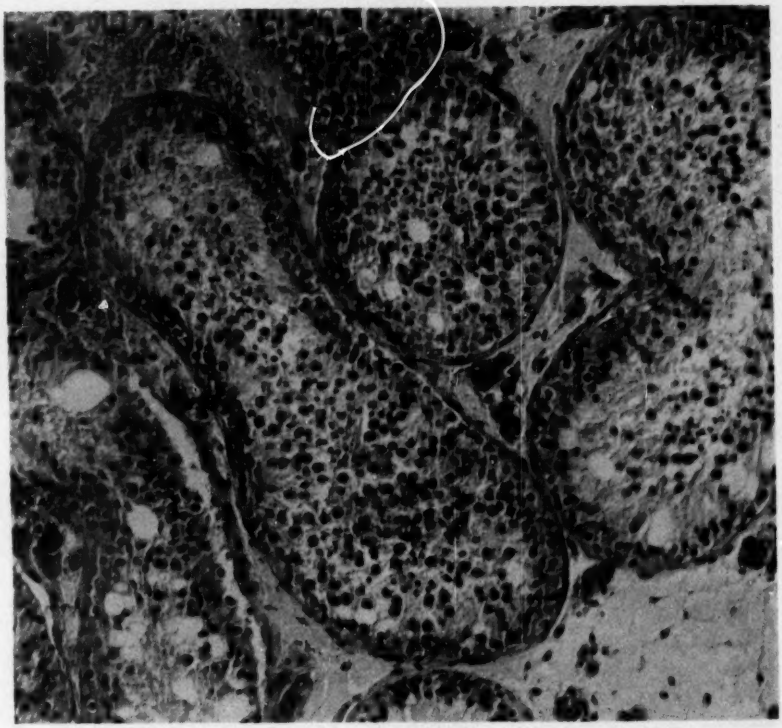

Fig. 2 (C. L., aged 37).—Testicular biopsy before treatment. Total sperm count was 6,500,000. There is arrest of spermatogenesis at level of spermatocyte stage in majority of tubules. Leydig cells appear normal.

(fig. 3). A man with oligospermia of undetermined etiology in whom the testicular biopsy reveals reversible changes in the germinal elements will react to the administration of testosterone propionate first with a further diminution of spermatogenic function, followed by a rebound phase after cessation of treatment which is characterized in a majority of instances by a striking increase in the number of spermatozoa (figs. 4 and 5). Furthermore, a comparison of the pretreatment biopsies with those made at the presumed height of the rebound phase shows that

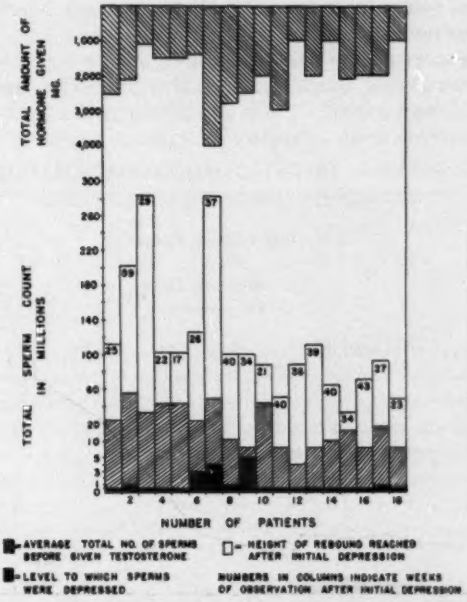
TOTAL AMOUNT OF HORMONE GIVEN MG.
TOTAL SPERM COUNT IN MILLIONS
NUMBER OF PATIENTS
AVERAGE TOTAL NO. OF SPERMS BEFORE GIVEN TESTOSTERONE
HEIGHT OF REBOUND REACHED AFTER INITIAL DEPRESSION
LEVEL TO WHICH SPERMS WERE DEPRESSED
NUMBERS IN COLUMNS INDICATE WEEKS OF OBSERVATION AFTER INITIAL DEPRESSION

Fig. 3.—Composite graph of 18 sterility patients treated with testosterone propionate, 150 mg. a week, which illustrates the striking increase in the number of spermatozoa over pre-treatment levels. Six of the patients have been reported on previously.

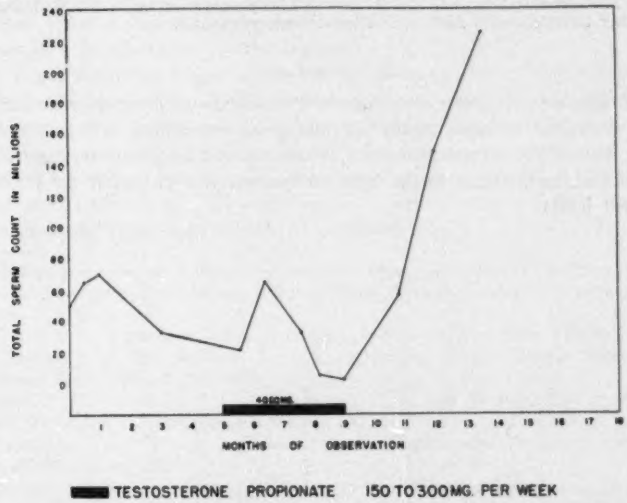

Fig. 4.—Spermiograph of M. T. Testicular biopsy is shown in figure 1. Note high rebound phase after treatment with 4,000 mg. of testosterone propionate.

the architectural pattern of spermatogenesis has not only improved but in some instances appears normal.

It is difficult at the present time to explain on a physiological basis the improvement in spermatogenesis which occurred after the initial androgen produced depression of tubules function. Also at the present time it is not known whether this response is specific to an androgenic substance or whether it can be elicited by other agents.

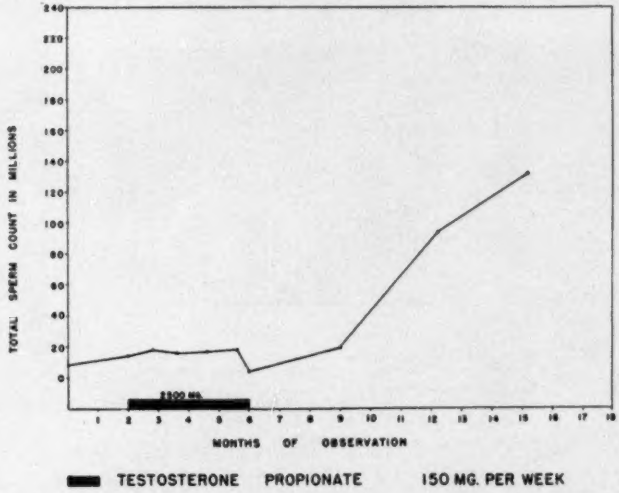

Fig. 5.—Spermiograph of C. L. Testicular biopsy shown in figure 2. Moderate rebound phase after treatment with 2,500 mg. of testosterone propionate.

SUMMARY

Testosterone propionate administered to subfertile men whose testicular biopsies reveal reversible changes in the spermatogenic mechanism will produce first a further diminution in the number of spermatozoa and then, after treatment has been discontinued, an increase in the level of spermatozoa so that it far exceeds pretreatment levels.

SUBTOTAL GASTRECTOMY COMPLICATED BY MINERAL DEFICIENCY, ESPECIALLY POTASSIUM DEFICIENCY

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AND
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THE PRIMARY purpose of this paper is to call attention to an unusual postoperative complication of subtotal gastric resection, namely, the development of a potassium deficiency state associated with hypochloremia and alkalosis of a severe degree. The etiology, symptomatology and therapy of this clinical syndrome are discussed, and a case is reported of an apparently moribund patient who recovered after recognition and adequate therapy of the deficiency state. Dr. Conley H. Sanford and Dr. Charles J. Deere, internists, referred this patient for surgical treatment and cooperated throughout the laboratory studies and the medical treatment.

The surgical literature contains relatively few articles regarding potassium deficiency, and references to potassium depletion and alkalosis as specific complications of gastric resection are limited. Recent presentations by Marks,[1] Kennedy and his associates,[2] Randall and his co-workers,[3] and Sedgwick [4] discuss the problems of potassium deficiency and the so-called hypochloremic alkalosis in the surgical patient, but none of these observers refer particularly to the importance of these conditions as a postgastrectomy complication.

The most important single factor in the development of the syndrome of hypopotassemia, hypochloremia and alkalosis following gastric resection is the loss of large quantities of gastric juice and bile through prolonged use of stomach suction or through vomiting. Prolonged suction following gastric resection is usually necessitated by malfunction of the gastroenteric stoma. Edema is the common cause of such malfunction. Roscoe Graham [5] cited a case in which the stoma failed to function for 43 days because of persistent edema.

From the Department of Surgery, University of Tennessee College of Medicine.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

1. Marks, L. J.: Potassium Deficiency in Surgical Patients, Ann. Surg. **132**:20, 1950.

2. Kennedy, T. J., Jr.; Winkley, J. H., and Dunning, M. F.: Gastric Alkalosis with Hypokalemia, Am. J. Med. **6**:790, 1949.

3. Randall, H. T.; Habif, D. V.; Lockwood, J. S., and Werner, S. C.: Potassium Deficiency in Surgical Patients, Surgery **26**:341, 1949.

4. Sedgwick, C. E.: Potassium Deficiency in the Postoperative Patient, S. Clin. North America **30**:799 (June) 1950.

5. Graham, R.: Surgical Therapy in Lesions of the Stomach and Duodenum, in Bancroft, F. W., and Wade, P. A.: Surgical Treatment of the Abdomen, Philadelphia, J. B. Lippincott Company, 1947.

Excessive loss of gastric juice and bile results in the loss of considerable quantities of potassium. According to Darrow,[6] gastric juice contains 30 mg. per 100 cc., or 8 milliequivalents of potassium per liter. Falconer [7] observed that vomitus contained five times the amount of potassium present in the serum. Similarly, large quantities of chloride ions are lost with the gastric juice. This chloride loss produces an excess of sodium ions, which in turn unite with bicarbonate to produce an excess of base and a state of alkalosis. The excess of sodium ions may also displace the potassium ions from the cells, allowing excretion of the potassium and thus further increasing the potassium deficiency. Loss of sodium in the gastric juice is of minor significance, as the relative loss is small and the excretion of sodium rapidly drops to negligible amounts when the intake is reduced to zero.[8]

Other factors influencing the development of potassium deficiency include lack of intake and continued excretion of the substance. The normal daily intake of potassium for an adult is about 3 to 4 Gm., or 75 to 100 milliequivalents.[8] Tarail and Elkinton [9] found that an adult on a potassium-free diet excreted 40 to 50 milliequivalents of potassium per 24 hours. Bellet and his associates [10] also indicate that potassium loss is accentuated in the presence of nitrogen loss and by parenteral administration of glucose.

The symptoms of alkalosis consist of changes in personality, delirium, slow, shallow respirations, stupor and, in some instances, muscle twitchings or convulsions.[11] Renal insufficiency may also accompany alkalosis.

The symptoms of potassium deficiency are varied, and since it is usually part of a multiple deficiency state and alkalosis, it is difficult to ascertain which symptoms are those of potassium deficiency and which are those of other deficiencies or alkalosis. Randall and others [3] divide the symptoms of potassium deficiency into two groups: (1) acute syndrome of skeletal muscle weakness, sometimes with paralysis of the intercostal muscles and diaphragm, and (2) insidious syndrome, the commoner type, with symptoms and signs appearing from the fourth to the ninth postoperative day. These symptoms include drowsiness, languor, chronic ileus with moderate distention, anorexia, weakness, peripheral edema, oliguria and hemoconcentration. In addition, myocardial failure with hepatomegaly, pulmonary edema and generalized edema are frequently observed in hypopotassemic states.

Webster [12] and his co-workers have recently shown experimentally that potassium deficiency leads to inhibition of the intestinal musculature and also to an increased secretion of gastric juice, with further potassium loss. Elman,[13] in discussing Webster's paper, referred to those patients with gastric retention in

6. Darrow, D. C.: Body Fluid Physiology: The Relation of Tissue Composition to Problems of Water and Electrolyte Balance, New England J. Med. **233**:91, 1945.

7. Falconer, cited by Bellet, S.; Nadler, C. S.; Gazes, P. C., and Lanning, M.: Effect of Vomiting Due to Intestinal Obstruction on the Serum Potassium, Am. J. Med. **6**:712, 1949.

8. Bodansky, A.: Parenteral Fluid Therapy, M. Clin. North America **34**:395, 1950.

9. Tarail, R., and Elkinton, J. R.: Potassium Deficiency and the Role of the Kidney in Its Production, J. Clin. Invest. **28**:99, 1949.

10. Bellet, S., and others: Am. J. Med. **6**:712, 1949.

11. Grace, W. J., and Barr, D. P.: Complications of Alkalosis, Am. J. Med. **40**:331, 1948.

12. Webster, D. R.; Henrikson, H. W., and Currie, D. J.: The Effect of Potassium Deficiency on Intestinal Motility and Gastric Secretion, Ann. Surg. **132**:799, 1950.

13. Elman, R., in discussion on Webster.[12]

whom organic evidence of obstruction seemed insufficient; he indicated that potassium deficiency might well play a significant part in the pathogenesis of such retention.

Electrocardiographic changes characteristic of alterations in serum potassium are described in the literature. According to Howard and Carey,[14] the electrocardiogram is the most practical aid to the detection of hypopotassemia and hyperpotassemia. Electrocardiographic changes indicating hypopotassemia consist of depressed, broadened T waves, prolonged Q-T interval and depression of the S-T segment. Other observers, including Elkinton and Tarail[15] and Darrow,[16] are of the opinion that these electrocardiographic changes, though not specific, are useful as supplementary data in the presence of altered serum potassium levels.

The recognition of hypopotassemia is not difficult if it is kept in mind as a possibility. Familiarity with the conditions likely to give rise to a potassium deficit, the presence of pronounced muscular weakness, electrocardiographic changes which disappear after potassium therapy and low serum potassium values should enable one to establish the diagnosis.

Once the diagnosis of hypopotassemia is made, therapy should be promptly instituted. Oral administration of potassium chloride is preferable though seldom feasible, since potassium deficiency is commonest in patients who cannot take food or drugs by mouth or in whom continuous gastric suction is being used. If oral administration is possible, 2 Gm. of potassium chloride may be given in fruit juice every four hours. The drug is also available in 5 grain (0.3 Gm.) tablets, which may be given in corresponding dosage. If oral therapy is not practicable, it may be given intravenously or by hypodermoclysis. Sterile potassium chloride salt may be added to any intravenous solution. Especially prepared 10 cc. ampules containing 20 milliequivalents, or 1.49 Gm., of potassium chloride are excellent for addition to standard solutions given intravenously. Darrow[16] recommends a solution containing 6 Gm. of sodium chloride and 2.7 Gm. of potassium chloride per liter for subcutaneous use.

It must be remembered that the intravenous use of potassium chloride is not without danger. Too rapid administration or the use of a too highly concentrated solution may lead to cardiac arrest and death. According to Howard and Carey,[14] the plasma reaching the heart must not contain more than 7 milliequivalents of potassium. These workers have given solutions containing from 40 to 90 milliequivalents of potassium at rates not greater than 180 drops per minute, the average being 120 drops per minute. Elkinton and Tarail[15] list a serum potassium level above 5.3 milliequivalents and renal insufficiency with oliguria as contraindications to administration of the substance.

The following case illustrates the syndrome of hypopotassemia and hypochloremic alkalosis complicating subtotal gastric resection with prolonged malfunction of the gastrojejunal stoma.

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14. Howard, J. E., and Carey, R. A.: The Use of Potassium in Therapy, J. Endocrinol. **9**:691, 1949.

15. Elkinton, J. R., and Tarail, R.: The Present Status of Potassium Therapy, Am. J. Med. **9**:200, 1950.

16. Darrow, D. C.: Body-Fluid Physiology: The Role of Potassium in Clinical Disturbances of Body Water and Electrolyte, New England J. Med. **242**:1014, 1950.

REPORT OF A CASE

W. E. B., a 56 year old white man, was admitted to the hospital on July 9, 1950, for surgical treatment of an obstructing duodenal ulcer. His past history was significant, in that during the three years preceding his admission he had undergone four operations. The last three of these were for a perforated diverticulum of the sigmoid colon and consisted of a laparotomy and loop colostomy, closure of the colostomy and surgical closure of the fistula in the sigmoid colon.

On July 11, 1950, a subtotal gastric resection with an anterior Polya anastomosis (Moynihan modification) was performed. Approximately two thirds of the stomach was removed, together with a contracted, deformed first portion of the duodenum and an adherent ulcer of the posterior wall. Adhesions from the previous operations, the deformity of the duodenum and fixation of the ulcer to the head of the pancreas increased the technical difficulty and resulted in more than the usual operative trauma in the region of the anastomosis.

The patient's early postoperative course was satisfactory. It soon became evident, however, that the gastroenteric stoma was not functioning properly. Attempts to discontinue the gastric suction after the third postoperative day were followed by vomiting of bile-stained fluid. On the ninth day, a roentgenogram revealed distention of the afferent jejunal loop and obstruction of the efferent loop.

TABLE 1.—*Serum Chemical Determinations*

Date	Potassium, mEq.	Sodium, mEq.	Chlorides, mEq.	CO_2 Combining Power, Volumes %	Proteins, Gm. per 100 Cc.	Nonprotein Nitrogen, Mg. per 100 Cc.
7/28/50	2.4	133.7	64.5	..	5.4	54
7/29/50	...	.....	.....	93	...	..
7/30/50	3.5	138	104	24	...	..
7/31/50	2.7	145	91.8	85	5.7	31
8/ 1/50	3.3	.....	.....	..	...	..
8/ 2/50	...	.....	.....	67	...	..
8/ 4/50	4.3	146	.....	..	...	..
8/ 8/50	3.9	148.3	113	..	...	..
8/11/50	...	.....	.....	42	...	..
8/15/50	4.7	143.5	114	..	...	..

The obstruction persisting, the abdomen was reopened on the eleventh postoperative day. The upper half of the wound was partially disrupted, the intestine was adherent to the anterior abdominal wall and there was diffuse thickening and edema of the wall of the small intestine. The stomach and the efferent loop of jejunum were also densely adherent to the undersurface of the liver, and the jejunal loop was angulated, but there was no organic obstruction. In the hope of promoting gastric emptying, an enteroenterostomy was performed between the afferent and efferent loops of the jejunum.

The patient did not improve after this procedure. Severe hiccough developed, and he complained of general discomfort and extreme weakness. His stomach still failed to empty, and large quantities of gastric juice and bile were lost through the stomach tube. The urinary output was adequate. He grew progressively worse, aphonia developed, he became confused mentally and went into a coma. On the seventeenth postgastrectomy day his condition was critical and he appeared to be almost moribund. Chemical studies of the blood on this date revealed potassium 2.4 millequivalents, chlorides 64.5 millequivalents and sodium 133.7 milliequivalents (table 1). The next morning the carbon dioxide-combining power of the blood was 93 volumes per cent. Intravenous administration of potassium chloride therapy was instituted, and in addition a 2 per cent solution of ammonium chloride was given to combat the alkalosis. The calculated dose of ammonium chloride to reduce the carbon dioxide-combining power from 93 to 50 volumes per cent, according to the method of Bodansky,[8] would have been 2,000 cc. of the 2 per cent solution; however, when 1,500 cc. had been given the patient exhibited signs of marked acidosis, with a respiratory rate of 72 and a carbon dioxide-combining power of 24 volumes per cent. This overcorrection of the alkalosis was temporary; by the next morning the carbon dioxide-combining power had risen to 85 volumes per cent.

From July 28 to August 12, the total amount of potassium chloride given intravenously was 49.17 Gm. The largest dose given during any 24 hour period was 7.45 Gm. The alkalosis gradually subsided as the potassium deficiency was corrected, and the intravenous therapy was varied as indicated. Within a week after the institution of the treatment, the patient became mentally alert and was able to understand conversation, though he could not yet swallow well and the aphonia persisted. His stomach still failed to empty.

Because of the persistent stomal malfunction, on the twenty-fourth postgastrectomy day a jejunostomy was performed for feeding purposes. The intraperitoneal reaction and the intestinal edema encountered at this time were much less severe than at the time of the enteroenterostomy, probably in response to the potassium therapy.

The patient's course after the jejunostomy was complicated by profuse gastric hemorrhage, with obstruction of the suction tube by clotted blood, vomiting of blood and signs of shock. The

TABLE 2.—*Summary of Fluid Intake and Output During Critical Period*

Date	Parenteral Fluids, Cc.	Enterostomy Feedings: Formula Plus H_2O, Cc.	Enterostomy Feedings: Gastric Aspirations, Cc.	Urinary Output, Cc.	Gastric Drainage, Cc.
7/28/50	3,500	.....	.....	2,340	.....
7/29/50	4,000	.....	.....	3,380	.....
7/30/50	5,700	.....	.....	1,850	3,800
7/31/50	6,000	.....	.....	1,600	3,350
8/ 1/50	4,500	.....	.....	1,770	4,100
8/ 2/50	5,500	.....	.....	2,550	3,130
8/ 3/50	4,500	.....	.....	2,370	2,650
8/ 4/50	3,000	.....	.....	2,025	2,395
8/ 5/50	4,000	.....	.....	1,500	1,505
8/ 6/50	5,050	320	.....	3,300	Unable to measure
8/ 7/50	2,000	1,150	.....	1,800	1,080
8/ 8/50	2,000	3,645	.....	1,780	1,350
8/ 9/50	3,000	3,850	.....	2,060	1,960
8/10/50	2,000	2,880	1,080	1,890	2,305
8/11/50	3,000	2,760	1,530	1,940	2,055
8/12/50	2,000	2,455	3,060 (700 cc. H_2O)	1,770	2,360
8/13/50	2,000	2,540	3,280 (510 cc. H_2O)	3,000	2,770
8/14/50	2,000	2,820	3,065 (465 cc. H_2O)	2,250	2,600
8/15/50	2,000	3,710	3,440 (570 cc. H_2O)	2,310	2,870
8/16/50	1,000	3,770	2,480	2,220	2,620
8/17/50	1,000	4,190	2,145 (90 cc. H_2O)	1,645	2,055
8/18/50	1,000	4,115	2,590	2,190	2,880
8/19/50	1,500	3,490	.....	1,370	.....

patient was also intensely jaundiced. After the institution of intravenous vitamin K therapy and topical administration of thrombin through the Levin tube, the bleeding ceased within 36 hours. From this time, his improvement continued. The greater part of the gastric juice and bile obtained by suction was returned to the intestinal tract through the jejunostomy tube. Potassium chloride was also given in this manner. From August 9 to 21, a total of 27 Gm. of potassium chloride was given through the tube. In addition, jejunostomy feeding was carried out according to the method of Case and his associates,[17] homogenized milk being used as a base (table 2).

On the thirty-first postgastrectomy day the patient had two dark stools, and the gastric drainage was considerably less profuse. Four days later, the serum potassium was 4.7 milliequivalents. A roentgenogram made on the thirty-seventh postgastrectomy day showed barium sulfate passing through both the gastroenteric stoma and the enteroenterostomy. Thereafter, the gastric suction was discontinued and the patient placed on a diet. The jejunostomy tube was removed on the forty-second postgastrectomy day, and he was discharged six days later.

17. Case, C. T.; Zollinger, R. M.; McMullen, C. H., and Brown, J. B.: Observations on Jejunal Alimentation, Surgery **26**:364, 1949.

COMMENT

It is probable that a large number of patients who undergo gastric resection show some degree of the deficiency state herein described. An extreme deficiency, such as the one reported here, however, is believed to be unusual. Randall and others [3] have recommended the prophylactic use of potassium intravenously in doses of 30 milliequivalents daily; such therapy might well be considered for patients who are maintained on gastric suction and parenteral administration of fluids for long periods.

Several features of this case merit special mention. Early postoperative edema of the stoma from trauma was later accentuated by both mineral and protein deficiency states. The institution of potassium chloride therapy, first intravenously and later through the jejunostomy tube, was followed by definite improvement in the patient's condition. The amount of potassium chloride given was determined by the patient's response, as indicated by repeated serum values and the clinical manifestations. Electrocardiographic studies were not made.

The gastric hemorrhage after the jejunostomy may have come from erosion of the lower portion of the esophagus by the Levin tube, which had been in place for 25 days, though it was believed to have come from the stomach. The jaundice and the low prothrombin level no doubt aggravated the hemorrhage.

The patient's improvement, once the stomach began to empty and food was taken by mouth, was dramatic. His progress has continued since his dismissal from the hospital, and recent roentgenograms demonstrated satisfactory emptying of the stomach and intestine.

DISCUSSION

DR. ROBERT L. SANDERS, Memphis, Tenn.: As surgical consultant in the case just presented and co-author of the paper, it was my privilege to learn firsthand about some of the effects of potassium deficiency. Dr. Gillespie was able to recognize the potassium deficiency state in this case from his previous investigative work in the hospital. Through his efforts and those of other observers, new light is being thrown on this matter, about which in the past we have been either in doubt or in error.

As we look back, probably all of us will recall having encountered these deficiency states, though without recognizing them. Just last night, Willis Gatch and I were discussing our experiences over the past 35 or 40 years, and we could remember many similar cases. Formerly, they were believed to be cases of mechanical obstruction, especially those wherein extensive edema of the tissues was found on exploration. We now know that edema is characteristic of a deficiency state.

All of us are indebted to Dr. Gillespie and others who are currently bringing this condition to our attention. Dr. Cole discussed the same problem yesterday. Now that we know potassium deficiencies may exist, we can be on the alert for the symptoms and promptly supply the lack in whatever amount is required.

DR. M. ZINNINGER, Cincinnati: I have no comments to make on potassium deficiency or the treatment of this case from that point of view, but I should like to emphasize the value of doing a jejunostomy for feeding purposes early in those patients who have difficulty in emptying through their stoma. It is a simple procedure to do and can be done with the patient under local anesthesia. Not only can you then give a mixture of homogenized milk or other substances, but you can take the material that you recover from the gastric suction, and refeed it into the jejunostomy, thus preventing loss of electrolytes and fluids.

DR. H. GLENN BELL, San Francisco: I want to cite one problem that we ran into with one patient recently. I believe I learned a lesson, and I shall never follow that procedure again.

A man of 65 had undergone a gastroenterostomy some 20 years before. He came in after a severe hemorrhage, and it took some time to get him in condition for surgical treatment. We operated on him perhaps a little earlier than we should have. Because his gastrojejunostomy had been done rather high up, I elected to do just a subtotal resection, take out his ulcer (which had been reactivated) and convert his stomach into a Billroth II type of anastomosis.

It did not function. On about the fifth postoperative day it was obvious from clinical and laboratory findings that severe acute pancreatitis had developed. His anastomosis did not function. We reoperated on him, and our anastomosis seemed to be all right. We did an enteroanastomosis, but still it did not function. We performed a jejunostomy in order to feed him, as he was showing a potassium deficiency but not to the marked extent in the case cited by the authors.

Subsequently I reoperated, undid the gastroenterostomy and the enterostomy and performed a subtotal resection on his stomach, which I should have done the first time. He recovered and in six months has gained 43 pounds (19.5 Kg.).

Dr. Edwin H. Ellison, Columbus, Ohio: We have been interested in this problem of potassium deficiency for about a year and a half. During that time routine determinations of serum sodium and potassium have been made in practically all the major surgical cases seen at the University Hospital. Interesting data in regard to subtotal gastric resection have come to light.

Prophylactic potassium therapy has seemed worth while. When the patient is admitted for a major gastric procedure he is given 2 or 3 Gm. of a mixture of potassium salts several times a day by the oral route. The mixture contains equal parts of potassium citrate, potassium acetate and potassium bicarbonate. A total daily dose of some 12 to 18 Gm. of potassium salts is given for three or four days prior to surgical intervention.

The postoperative courses after 36 subtotal gastric resections for ulcer have recently been reviewed. The average hospital stay after subtotal resection in patients who had received prophylactic potassium was nine days and in those who did not receive this it was 13 days. In general the longer stay resulted from problems of distention of poorly functioning gastroenterostomy stomas.

Other interesting observations have been made regarding muscle and red cell potassium. At the time of operation a small segment of rectus muscle is removed, and the contents of muscle potassium in the muscle tissue is determined. Normal values in our laboratory approximate 100 milliequivalents. Muscle potassium levels have seemed to have some prognostic value. If the muscle potassium is found to be low, even though the blood serum levels are normal, the patient's total body potassium is considered low and intensive replacement is started.

The study of red cell potassium has also proved of interest. As I recall, Dr. Cole in his presidential address this morning pointed out that sodium replaces potassium in the cell. The measurement of the red cell potassium has helped us to study this phenomenon. In general, patients demonstrating a fall in serum potassium showed a parallel decrease in red cell potassium. The clinical significance of red cell potassium is still under study.

Repeated electrolyte studies in the period immediately after operation has shown that the average patient has a drop of about 1 milliequivalent of serum potassium during the first six days after surgical intervention. The usual patient on gastric suction or taking nothing by mouth is given 30 milliequivalents of potassium, supplied as 2.23 Gm. of potassium chloride daily by the intravenous route. We have found it convenient to keep autoclaved bottles of measured amounts of potassium chloride readily available. When an infusion is to be given, the contents of the bottles are dissolved in 20 cc. of distilled water and introduced in 1 liter of the selected fluid. Oral potassium therapy, in diminishing amounts, is instituted as soon as the patient is able to take fluids by mouth. In most instances this plan of therapy maintains the serum levels at normal values and successfully prevents the troubles of potassium deficiency.

Dr. Clarence E. Gillespie, Memphis, Tenn.: I wish to thank the discussers for their remarks and viewpoints, especially those with reference to potassium therapy and the prophylactic use of potassium salts in surgical patients.

The value of jejunostomy in this case should be emphasized, and, looking back on the progress of the patient discussed, I feel that this procedure probably should have been done earlier than it was. A jejunostomy at the time of gastrectomy would have allowed early alimentation and undoubtedly would have prevented the deficiency state responsible for the stormy postoperative course of our patient. At the time of reoperation, when the enteroenterostomy was performed, a jejunostomy might also have been done, but it is questionable whether it would have functioned with the thick, leathery bowel which was encountered. The condition of this bowel and the general state of the body tissues was much improved after potassium and other replacement therapy, and when the peritoneal cavity was reentered for the purpose of doing the jejunostomy the condition of the intestine was such that a return of peristalsis and good function of the jejunostomy could be reasonably expected. Favorable response accompanied jejunal alimentation with refeeding of the gastric aspirations and administration of potassium chloride through the jejunostomy tube.

The total amount of potassium administered in this case was approximately 50 Gm. intravenously over a period of 16 days and 27 Gm. through the jejunostomy stoma over a period of 13 days. The dramatic response to oral feeding usually described in the potassium-deficient patient was noted as soon as this patient was able to take food by mouth.

HASTENING OPERATIVE EXCLUSION FOR FISTULA OF EXTERIORIZED ILEUM OR JEJUNUM

E. LAWRENCE KEYES, M.D.
ST. LOUIS

EXPERIENCE indicates that 22 days ordinarily elapse from the time of exteriorization of the small bowel until the performance of the operation of complete exclusion for the control of the resulting fistula. The time will be shortened as one gains confidence in the exclusion operation, and Middleman [1] has successfully reoperated as early as the fifth day after exteriorizing gangrenous ileum. To wait as long as 47 days, for instance, after exteriorizing gangrenous ileum before excluding the resulting fistula seemed to Probstein [2] "what I now feel much too long a time," so that when next he had occasion, after exteriorizing jejunum, to use the exclusion operation, he waited only 14 days. The urgent need for hastening the exclusion operation for the control of jejunal or ileal fistulas is therefore the topic of this presentation.

Timing the Exclusion Operation

Interval		Surgeon	Interval		Surgeon
1. Jejunal or High Ileal Fistulas			2. Low Ileal Fistulas		
9 days 14 days 22 days 30 days 34 days	22 days—average	Cokkinis * Probstein Keyes † Middleman † Keyes	5 days 15 days 47 days	22 days—average	Middleman Keyes Probstein

Time—from exteriorization to exclusion. All 8 patients survived. Bowel gangrenous in all but one patient.

* Cokkinis, A. J.: Postgraduate Surgery, edited by R. Maingot, New York, Appleton-Century-Crofts Company, 1936, pp. 1056-1065.
† Keyes, E. L., and Middleman, I. C.: Surg., Gynec. & Obst. **72**: 237, 1941.

How long a patient may be expected to survive exteriorization of gangrenous small bowel without the employment of the exclusion operation for the control of the resulting fistula may be judged from the fact that death occurred in 12 days

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From St. Louis University School of Medicine, Department of Surgery, and the Jewish, St. Luke's, Homer G. Phillips, and St. John's hospitals.

1. Middleman, I. C.: Personal communication to the author (1950).

2. Probstein, J. G.: Value of the Exclusion Operation in the Treatment of Intestinal Fistulas, Surgery **20**:233-236 (Aug.) 1946. Cokkinis, A. J.: Postgraduate Surgery, edited by R. Maingot, New York, Appleton-Century-Crofts Company, 1936, pp. 1056-1065. Keyes, E. L., and Middleman, I. C.: The Treatment of Fistula and Obstruction of the Small Intestine by Complete Exclusion, Surg., Gynec. & Obst. **72**:237-243 (Feb.) 1941.

in a young woman after exteriorization of gangrenous jejunum and in 64 days in an elderly woman after exteriorization of gangrenous ileum. In both patients the usual supportive measures were used, such as oral and intravenous alimentation, replacement of secretions from the proximal into the distal loop of the fistula and spur crushing; in neither patient was the exclusion operation employed, and neither patient, in consequence, survived.

Temporizing by spur crushing or by performing enteroenterostomy deep to the fistula merely delays matters, and Dixon [3] warns that "it is foolish to attempt to close a fistula if the bowel distal to the point of origin is subacutely or completely obstructed." Cokkinis in 1936 unsuccessfully tried enteroenterostomy deep to exteriorized ileum in an elderly man, who rapidly failed until the performance on the ninth day of the complete exclusion operation on the advice of Professor Pannet.

Exclusion procedures, incidentally, were described in 1888 by Trendelenburg [4] and were used for regional enteritis in 1936 by Ginsburg.[5] In 1939 I tried one for the first time for the control of a high ileal fistula following exteriorization of gangrenous ileum strangulated in a hernia, and in the past decade more than 30 successful exclusion operations have been performed by surgeons in St. Louis alone. Wu [6] notes the common use of the procedure in China after incision of gangrenous strangulated external hernias resulting in fistulas, and Gatch [7] has devised an interesting variant of the procedure employing Miller-Abbott tubes. Dixon considers the exclusion operation "a very valuable form of treatment for persons who have persistent external fecal fistula," particularly "those whose general condition is so poor that a more extensive operation would be unduly hazardous. A preliminary short-circuiting procedure [exclusion] may allow a striking improvement in general health." Nowhere in the literature, however, is stressed the urgent need for undelayed employment of exclusion for control of a complete external fistula of the small bowel (fig. 1).

The chemical background for the rapid deterioration of patients with fistulas following exteriorization of gangrenous jejunum or ileum may be summarized by recalling that there is a loss to the patient via the fistula of most of the 5 to 7 liters daily secreted by pancreas, liver, stomach and small intestines. Loss of the secretions of the pancreas and liver has been shown by Elman and McCaughan [8] to be incompatible with life for dogs, despite fluid and electrolyte replacement. Alkalosis and loss of sodium and potassium soon result from fistula. Unless the continuity of the intestine is restored by operation, and restored very soon after the fistula forms, the patient will die; restoration of intestinal continuity is accomplished either by the complete exclusion operation or by excision of the fistula and reanastomosis.

3. Dixon, C. F., and Benson, R. E.: Principles in the Management of External Fecal Fistulas, J. A. M. A. **130**:755-761 (March 23) 1946.

4. Trendelenburg, in Guillermo, E. M.: Unilateral Intestinal Exclusion, Surg., Gynec. & Obst. **36**:773-776 (May) 1923.

5. Ginsburg, L.: Persistent Abdominal Fecal Fistulas Due to Regional Ileitis, Surgery **7**:515-528 (April) 1940.

6. Wu, Y. K.: Personal communication to the author (1942).

7. Gatch, W. D., and Montgomery, W. F.: The Treatment of External Hernias Containing Gangrenous Bowel: New Method Utilizing the Miller-Abbott Tube, J. A. M. A. **129**:736-739 (Nov.) 1945.

8. Elman, R., and McCaughan, J. C.: The Fatal Effect of the Complete Loss of Pancreatic Juice, Proc. Soc. Exper. Biol. & Med. **24**:99-101 (Oct.) 1926.

Patients with fistulas after exteriorization of gangrenous ileum or jejunum deteriorate rapidly probably because they were at first already in chemical imbalance, owing to initial acute obstruction of the ileum or jejunum. These patients will not long tolerate a complete external fistula even low in the ileum, probably because the emptying time of the intestine becomes much accelerated after emergency exteriorization of the ileum. Patients with fistulas after ileostomy for such chronic disease as ulcerative colitis or extensive polyposis of the colon, on the other hand, can tolerate indefinitely a complete external fistula of the ileum, probably because in these patients the ileum has gradually and over long periods taken over from the colon much of its absorptive function.

To summarize the chemical versus the operative view of curing complete external jejunal or ileal fistulas following exteriorization, one must urge early operative

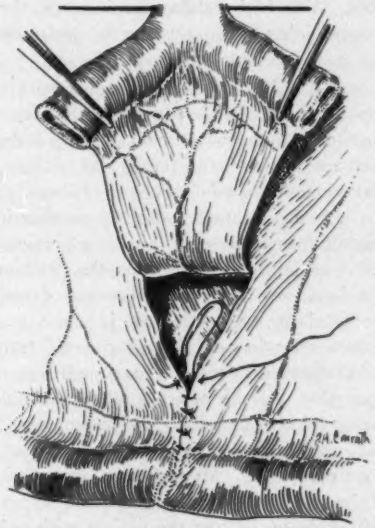

Fig. 1.—Complete exclusion of fistula in jejunum. Jejunoileostomy short-circuits fistula completely. Fistulous bowel nourished by its intact mesenteric vessels. With long excluded defect, leave large defect in mesentery. With shorter defect, close defect completely; never leave defect small. With long excluded defect, exteriorize ends of fistulous bowl, shown clamped. With short excluded defect and purse-string ends, drop ends back but drain blind fistula externally unless it is wide open.

restoration of anatomical intestinal continuity as a better way of building up the patient for operation than the use of chemical aids.

Exclusion operations are of various types. High fistulas, i. e., those arising from the jejunum or high in the ileum, can be treated by jejunoileostomy, sometimes by jejunocolostomy. Low fistulas, i. e., those arising from the last loops of ileum, can be treated by ileocolostomy. Exclusion should be complete and not partial. The excluded segment of bowel can be removed subsequent to exclusion or left in situ for 10 years.

The level of the fistula had best be determined preoperatively by introducing barium sulfate directly into the fistula under the fluoroscope, a more instructive

procedure than making a series of roentgenograms of the upper gastrointestinal tract after giving barium sulfate by mouth. Passing barium sulfate into the distal loop of the fistula enables the radiologist and the surgeon to ascertain whether the fistula arises in the jejunum or in the ileum and also whether or not the fistula communicates with the colon. Should the fistula be an intestinovaginal one, as in a patient of mine [9] and in one of Heifetz',[10] both of whom had previously been irradiated for uterine or cervical carcinoma, a rectal tube can be passed up through the vault of the vagina into the fistula and barium sulfate introduced into the tube to determine the level of the fistula. In both these patients double fistulas were found, i. e., ileovaginal and sigmoidovaginal fistulas, all defecation occurring per vaginam and not per rectum. Barium enema aids in cases of this sort also.

The choice of operation should be tentatively fixed in mind before the exclusion operation is undertaken. With high fistulas, for instance, those in the jejunum as in the case reported here, jejunoileostomy may be performed provided the ileum is free from adhesions, abscesses and secondary fistulas.

With high fistulas, one may be faced with the question of how much small bowel may be excluded without detriment to the patient. In the patient to be discussed here I performed jejunoileostomy with complete exclusion of the jejunal fistula from enteritis, leaving in situ approximately 18 inches (45 cm.) of jejunum distal to the ligament of Treitz plus some 42 inches (106 cm.) of ileum proximal to the cecum, a total of only 5 feet (152 cm.) of small bowel. In another instance, Elman,[11] also faced with a jejunal fistula from enteritis in a patient previously operated on, could find but 3 feet (91 cm.) of jejunum free within the peritoneal cavity beyond the ligament of Treitz; the ileum was inaccessible because of a mass of adhesions. He therefore excluded the fistula by transecting the jejunum, anastomosing the proximal jejunum to the transverse colon and dropping back intraperitoneally the purse-stringed distal loop of transected ileum, thus accomplishing jejunocolostomy with partial exclusion. After nine days he resected all the excluded intestine from the jejunum to the transverse colon, thus leaving the patient with but 3 feet (91 cm.) of functioning jejunum attached to the left side of the colon. The patient recovered and returned to his previous occupation. In a woman with carcinoma of the jejunum, Jackson [12] resected all the small intestine except about 8 inches (20 cm.) of jejunum and 4 inches (10 cm.) of ileum, leaving the patient with only 1 foot (30 cm.) of functioning small bowel; she recovered her normal weight and was alive six months postoperatively. It is true that she had no fistula, but the case is referred to merely to show how little small intestine, i. e., from 1 to 3 feet (30 to 91 cm.), can be left in situ compatible with life for the patient.

With low fistulas, i. e., those from the last loop of ileum, ileocolostomy is preferable to ileoileostomy. For example,[9] in a woman with an ileovaginal fistula following irradiation of uterine carcinoma, I transected the ileum both above and below the

9. Keyes, E. L.: Further Experience with the Exclusion Operation for the Treatment of Fistula of the Small Intestine, South. M. J. **35**:832-837 (Sept.) 1942.

10. Heifetz, C.: Personal communication to the author (1950)

11. Elman, R., and Read, J. A.: Nutritional Recovery Following Removal of All But 3 Feet of Jejunum and Half the Colon, J. Missouri M. A. **42**:145-146 (March) 1945.

12. Jackson, J. A., in discussion on Clark, O. R., and Mills, W. M.: Repeated Massive Intestinal Hemorrhage from Multiple Malignant Tumors of the Jejunum, Tr. West. S. A. **56**:170, 1949.

fistulous bowel, only to find the stub of distal ileum retract so far that ileocolostomy was performed in preference to the contemplated ileoileostomy. The excluded segment of terminal ileum was resected on completion of the anastomosis, but had it been left in situ as an excluded segment a drain would have had to be passed up through the vagina into the fistulous bowel and kept in to avoid postoperative closed loop obstruction of the excluded loop of fistulous ileum. In another patient, a man with a fistula of the ileum after a gunshot wound of the abdomen, Heifetz [10] merely did ileocolostomy after transecting the ileum afferent to the fistula and dropping the purse-stringed afferent stub of ileum back intraperitoneally. This procedure left the patient with a partial type of exclusion, no drains being necessary into the excluded loop, so large were the communications from the ileum to the abdominal wall. Exclusion was successful as a partial rather than a complete type of procedure because the ileocecal valve was competent.

In patients whose ileocecal valve is incompetent, or lacking as after right hemicolectomy, or by-passed after previous ileocolostomy, ileal fistulas must be completely and not partially excluded or else trouble will ensue. For example, I did ileosigmoidostomy to control successfully a fistula high in the ileum.[2] The ileosigmoidostomy was accompanied with transection not only of the ileum but also of the sigmoid loops which attached to the fistula, for the patient lacked an ileocecal valve, having previously undergone right hemicolectomy for regional enteritis. Had the exclusion been partial and not complete in type, intestinal contents would have kept draining outwardly via the colon and the patient would have, at most, only been improved. Harbison [13] discovered this complication in operating on a patient for ileal fistula after a previous ileocolostomy. He first performed ileocolostomy with partial and not complete exclusion and later had to reoperate because of reflux of ileal contents through the colostomy and make the exclusion complete by severing the attached loop of colon before the patient recovered (fig. 2).

The loop of fistulous intestine may blow out when excluded completely unless it is short and drains freely to the outside of the body. This occurred in a patient of mine, a young woman, because I failed to exteriorize the colon to allow external drainage of a long fistula of the ileum. North [14] "came to grief by failing to exteriorize both ends of an excluded segment of intestine, the seat of regional ileitis, blind loop obstruction having developed in the excluded intestine." Webb [15] avoided a closed loop obstruction by catheter drainage of an excluded fistulous ileum. Kidd [16] was just able to avoid closed loop ileal obstruction by means of early postoperative ambulation to induce profuse discharge on the abdomen of mucus from the excluded fistulous segment of ileum.

The excluded loop of intestine may be left in place as long as 10 years as a blind on mucous fistula, as with two patients of mine, operated on in 1939 and 1940; it may be removed nine days later, as in Elman's case referred to above, or any time thereafter, or it may be removed immediately on completion of the anastomotic phase of the exclusion operation, as in a patient of mine in 1942.

13. Harbison, S. P.: The Principle of Complete Exclusion in Fistulas of the Small Intestine, Surgery **28**:384-392 (Aug.) 1950.

14. North, J. P.: Personal communication to the author (1950).

15. Webb, C. E.: Personal communication to the author (1950).

16. Kidd, F. H.: Personal communication to the author (1950).

Before operation is performed on a patient for fistula, these points may be recalled: Robinson [17] indicates that "a patient with a newly working ileostomy should receive as nearly as possible an amount of Hartmann's solution or isonate solution equivalent to the amount of drainage from the ileostomy," which may reach 4 to 6 liters daily. "If able to take fluids by mouth, part may be replaced through the use of sodium bicarbonate, sodium chloride solution" consisting of "sodium chloride three grams plus sodium bicarbonate one and one-half gram in one liter of water." A fistulous patient avidly requests this bicarbonate solution. It should be supplemented by beef broth which is rich in potassium. Potassium is given in

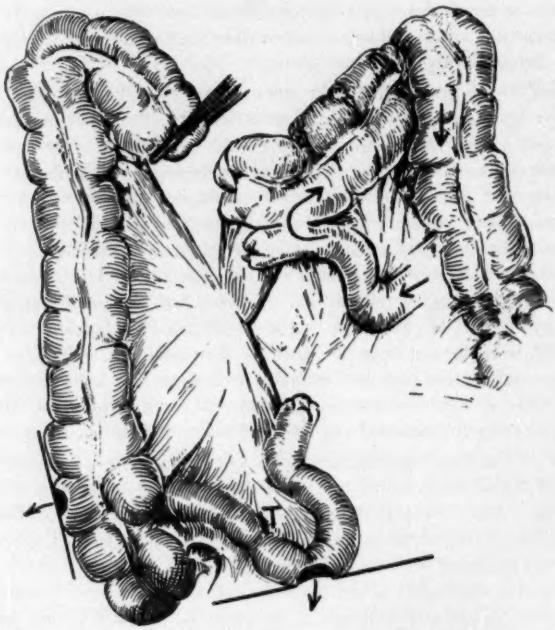

Fig. 2.—Complete exclusion of fistula of both ileum and colon. Ileocolostomy, with transection of colon, to make exclusion complete. Transection of colon unnecessary if colon not fistulous. Exteriorize clamped end of colon to avoid blowout. With lengthy deep fistula, drain blind fistulas also. (Redrawn from figure in a previous article, South. M. J. **35**:832 [Sept.] 1942.)

2 to 3 Gm. doses daily if the patient cannot eat, daily potassium blood levels being used as a guide to prevent potassium poisoning (Cole [18]). Kidd found a carbon dioxide-combining power of 34 per cent in a fistulous patient on the eve of an exclusion operation, which he brought to a normal 53 per cent by administration of 2,000 cc. of one-sixth molar sodium r lactate solution intravenously up to mid-

17. Robinson, J. R.: Recent Developments in Water Balance, Am. J. Surg. **76**:383-392 (Aug.) 1948.

18. Cole, W. H.: The Use of Laboratory Aids in Surgery with Special Reference to Potassium Deficiency, Tr. West. S. A., 1950, to be published.

night. Replacing fluids from proximal into distal loops, while helpful, generally fails to maintain nutrition. The part played by amigen,* blood, vitamins and antibiotics is well known.

REPORT OF A CASE

Example of the Complete Exclusion Operation.—Mr. H. G., aged 45, had postoperative eventration after laparotomy for regional enteritis. A complete external fistula of the jejunum developed in the right rectus incision, and the patient failed rapidly despite intensive oral and intravenous alimentation including administration of amigen.* After a delay of 34 days, occasioned by lack of comprehension of the value of the exclusion operation, on Feb. 26, 1947, complete exclusion of 15 feet (457 cm.) of jejunum and ileum, and jejunoileostomy were performed.

The purpose of operation was to anastomose normal intestine after its complete severance with the fistulous small bowel, to exclude the fistulous bowel completely from the fecal circuit and at a later stage to resect the diseased intestine, should the patient so desire.

A transverse incision was made, beginning in the left upper quadrant. Peritoneum was entered over the ligament of Treitz in a field free from adhesions. Two feet of jejunum intervened from the ligament of Treitz and the external fistula of the jejunum. Massive adhesions were encountered about the fistulous segments of jejunum and ileum, with matted intestine and enlarged mesenteric nodes. Knowing that 18 inches (46 cm.) of jejunum was adequate for life, the plan was to do the exclusion as a jejunotransversecolostomy. First, however, the cecum was sought, and 4 feet (122 cm.) of collapsed but otherwise normal ileum was found between the cecum and the mass of adhesions. Consequently the plan was changed and jejunoileostomy performed, as follows.

The jejunum was transected 18 inches (46 cm.) from the ligament of Treitz. The ileum was transected 3½ feet (107 cm.) from the cecum. The proximal jejunum was anastomosed to the distal ileum (fig. 1). Because 15 feet (457 cm.) of jejunum and ileum was excluded and left in attached to its mesentery whose root was 8 inches (20 cm.) long, a defect had to be left in the mesentery; this defect was purposely left large to avoid postoperative strangulation of a loop of ileum through a remaining small defect (fig. 1), such as had occurred in the mesentery of a previous patient, causing her death after exclusion. To strengthen the mesentery adjacent to the newly sutured bowel, the anastomosis was made side to side and not end to end, in order to overlap mesenteries.

Finally the jejunal and ileal ends, indicated in figure 1 as held in clamps, were both exteriorized to prevent secondary blind loop obstruction within the 15 feet of excluded small intestine, and the wound was closed.

The patient made a dramatic recovery, and after five months of increasing adiposity insisted that Dr. Heifetz resect the 15 feet of excluded loops of jejunum and ileum. Resection of this was successfully accomplished at that time.

Comment.—Notice that the incision was transverse, beginning in the left upper quadrant. In other patients a left rectus incision may be preferred, beginning also in the left upper quadrant.

The ligament of Treitz is the first structure sought when the abdomen is opened in order to identify jejunum and follow it down to the adhesion about the fistula. This identifies with certainty the proximal loop entering the fistula and is easier than the original method of inserting catheters of different sizes into the fistula to identify loops. Harbison prefers a Miller-Abbott tube to identify the proximal loop.

The distal loop is identified by following the ileum from the cecum upward to the adhesions about the fistula.

The closure of the defect in the mesentery is important (fig. 1). If a long segment of intestine, such as 15 feet of jejunum and ileum, is to be excluded, it is better to leave a large defect in the mesentery rather than a small one. A large

defect is less apt to lead to postoperative strangulation of ileum through the defect, such as caused death in a patient of mine. However, it is preferable, if possible, to close the defect in the mesentery entirely.

Side to side anastomosis of jejunum to ileum was employed here, with overlap of mesenteries to strengthen the anastomotic line above the defect which remained in the mesentery. Other surgeons such as Heinbecker and Kidd have used end to end anastomosis, but this is to be avoided unless the entire defect in the mesentery can be closed. In anastomosing ileum to colon I preferred end to side rather than side to side anastomosis, as illustrated in figure 2.

The exclusion operation is lifesaving. Of nine patients on whom I have operated, three have died. Other surgeons in St. Louis have had better results, although in smaller individual series of cases. All eight patients listed in table 1 are living. It is important to remember that death in such patients is due to chemical imbalance resulting from the fistula rather than from the exclusion operation.

SUMMARY

The exclusion operation for the cure of fistula resulting after exteriorizing jejunum or ileum is lifesaving. However, it should be used within three weeks of exteriorization and may be used as soon as the fifth day. To wait a month or two is to endanger unnecessarily the life of the patient who has a complete external fistula of the small bowel.

DISCUSSION

DR. J. PROBSTEIN, St. Louis: My interest in this subject really came about, first, because of the campaign that Dr. Keyes had carried on in and around St. Louis advocating this method of procedure, and, second, because of the first case I encountered several years ago, in which I was compelled to use this method to save the patient.

The first patient was a 23 year old woman who was eight months' pregnant. She was admitted to the hospital, and for one week the diagnosis was not determined. On the eighth day she vomited fecal material, and it was obvious that there was obstruction.

[Slide] Some of you may have seen this slide, and I ask your pardon for its repetition. On the eighth day we operated. Opening the abdomen, we noticed that there was a band across a loop measuring about 15 cm. This loop was gangrenous. There was some difficulty in reaching the site because of the eight month pregnancy. When the band was released, the loop of bowel fell into the abdominal cavity. The band practically transected this loop, so I was left with the open ileum and the small piece of ileum attached to the cecum, which measured about 3 cm.

I exteriorized the gangrenous loop and pulled the cecum up with the ileum, and, as you see here, this part measured about 3 cm. When I completed the procedure the cecum and the ileum were out on the skin, giving both a small bowel fistula and a large bowel fistula.

We went on for about 46 days trying to establish the electrolyte balance before exclusion was considered. As Dr. Keyes mentioned, instead of doing an immediate exclusion we used the conservative procedures, such as suction, etc.; the electrolyte balance was not maintained, and it looked as though we were going to lose the patient.

Someone asked me if I thought we might try Keyes' exclusion operation. We reoperated and separated the ileum, brought the end up to the transverse colon and left the small blind loop. We completely excluded the large bowel, and because this part was practically open, not leaving a closed ileocecal valve, a blowout did not occur. The result was dramatic. Within 48 hours the patient looked like a new person and went on to a rapid recovery. She came back several months later, at which time we removed this segment of bowel in its entirety.

The next case was more recent. A patient was admitted to the Homer Philips Hospital who had obstruction in which there was a gangrenous loop. The loop was exteriorized.

[Slide] On the day of operation this patient became oliguric and for six days did not pass more than 350 cc. of urine. In other words, a typical lower nephron syndrome developed.

All during this time she had a draining fistula. She was treated for the lower nephron insufficiency and about the thirteenth postoperative day started to put out sufficient urine. Although the nonprotein nitrogen was then 67 mg. per 100 cc., it was considered wise to do the exclusion operation.

I have here the two catheters which we used in our third case, one a large catheter and one a small catheter, because we think we can more easily identify the efferent and the afferent loops. We excluded the two small pouches of ileum. We reunited the small bowel, and when the patient came back about three and a half weeks later we removed the two blind pouches. She has been perfectly well since.

I have had five patients with this type of condition, all of whom have become well without difficulty and without any deaths in this small series. I believe the procedure is of value in this type of case and maybe a lifesaving measure.

Dr. Charles W. Mayo, Rochester, Minn.: I take it, from the description of the cases and the subject matter of his paper, that all these patients are very sick. If you have done the primary operation for a strangulated piece of bowel, you realize that it has been accomplished by a competent surgeon! If, on the other hand, the patient comes to you with a double-barreled jejunostomy or ileostomy, you may question whether the primary operation has been done by a competent surgeon. You may feel that it might better have been accomplished with primary resection of the gangrenous piece of bowel or that exteriorization of the gangrenous piece of bowel should have been done, but at the same time ileoileostomy or jejunoileostomy, side to side, should have been performed intraperitoneally so that fluids would not be lost.

I know that there are situations which require the type of operation that Dr. Keyes has described, and I realize that in some instances it is a lifesaving measure. As time goes on, however, it is to be hoped that continued improvement in the preparation of patients for operation and continued development of surgical technic, as well as refinement in postoperative care, will bring most of the conditions that previously have required multiple stage procedures into the realm of single stage operations.

Dr. J. Dewey Bisgard, Omaha: Several years ago Dr. Eric A. MacNaughton, a surgeon at the Montreal General Hospital, presented an apparatus and device by which one can transport the secretions from the fistula of the proximal loop across into the distal loop. This is a lifesaving procedure and is applicable in fistulas of the duodenum, such as blown out duodenal stumps or when a diversion operation as described by Dr. Keyes is not possible.

I should like to show you a picture of this apparatus, in case some of you are not familiar with it.

[Slide] This shows its application to the exteriorized ends of a strangulated, gangrenous loop of bowel which had perforated and caused diffuse peritonitis. This constant running suction pump creates in this gravity bottle a negative pressure which draws up the secretions from the sump arrangement in the proximal end and drops them into the top of the gravity bottle. They then drop to the bottom and run by gravity into the distal loops. The apparatus can be applied to all types of small bowel fistulas.

I have had three patients with duodenal fistulas who have recovered when this procedure was used. In these cases a jejunostomy was done to give access to a distal loop to receive the transported secretions. Also with this apparatus supplementary feedings and the necessary fluids can be given into the gravity bottle to flow into the distal loop.

Dr. E. Lawrence Keyes, St. Louis: The exclusion operation is not applicable to duodenal fistulas. I think the apparatus as shown seems good for duodenal fistulas, and I should like to comment on the fact that one of our patients was kept alive by the use of a rather similar apparatus for a number of months. I still feel that operation is the best means of treatment of small bowel fistulas, however, and not the use of gadgets.

RETROPERITONEAL TUMORS IN INFANTS AND CHILDREN

Report of Eighty-Eight Cases

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CHARLES A. KRUSE, M.D.
E. M. GREANEY, M.D.
AND
LAWRENCE CHAFFIN, M.D.
LOS ANGELES

THIS PAPER is the outcome of a study of the case histories of all infants and children with the final diagnosis of a retroperitoneal tumor admitted to the Los Angeles Childrens Hospital during the years 1936 to 1950.

Farber [1] and others [2] have recently discussed these tumors collectively, on the basis of the region of origin and certain common clinical findings. The latter aspect of the subject was particularly manifest as this survey progressed. Without the surgical report, or pathological findings, it was impossible to determine accurately the nature of the tumor in a majority of the cases studied. Since retroperitoneal growths form by far the most frequent abdominal tumor of childhood, they are often encountered by the general surgeon. With earlier diagnosis, and improved methods of treatment, cure can be anticipated in about one third of the cases (Wittenborg [3]; Neuhauser [4]). These facts have led to a renewed interest in these tumors and to the following analysis. (See tables 2, 5 and 6.)

MATERIAL

There were 88 retroperitoneal tumors (table 1) diagnosed at the Los Angeles Childrens Hospital between the years 1936 and 1950. Each chart has been carefully reviewed and the information tabulated for this survey. The final diagnosis was established in every case by

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Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

From the Department of Surgery, University of Southern California Medical School, and the Childrens Hospital.

1. Farber, S., in discussion on Case Records of the Massachusetts General Hospital, Case 27392, New England J. Med. **225**:510, 1941; Tumors in Early Life, in Nelson, W. E.: Textbook of Pediatrics, Philadelphia, W. B. Saunders Company, 1950, p. 426.

2. (*a*) Pilcher, F.: Retroperitoneal Tumours in Children, Canad. M. A. J. **48**:505, 1943. (*b*) Hansmann, G. H., and Budd, J. W.: Massive Unattached Retroperitoneal Tumors: Explanation of Unattached Retroperitoneal Tumors Based on Remnants of Embryonic Urogenital Apparatus, J. A. M. A. **98**:6 (Jan. 2) 1932.

3. Wittenborg, M. H.: Roentgen Therapy in Neuroblastoma: A Review of 73 Cases, Radiology **54**:679, 1950.

4. Neuhauser, E. B. D., cited by Harvey, R. M.: Wilms' Tumor: Evaluation of Treatment Methods, Radiology **54**:689, 1950.

the pathologist, either from the surgical specimens or from the autopsy. All cases have been followed to the present time. Members of the Childrens Hospital staff cooperated fully in making these cases available for study. (Dr. Carl Rusche, of the Urological Service of this hospital, has published an excellent separate article which included most of the Wilms tumors studied in this series. He has very kindly made these cases available.)

TABLE 1.—*Classification of Retroperitoneal Tumors*: Series of 88 Consecutive Cases from Los Angeles Childrens Hospital*

Type	Total Number	Percentage
Embryoma of kidney or Wilms's tumor	47	53.4
Fibrosarcoma	1	....
Rhabdomyosarcoma	1	....
Myxofibroma	1	....
Adult teratoma (benign)	1	....
Extensive lipoma (benign)	1	....
Neuroblastoma	31	35.2
Sarcoma, undifferentiated	1	....
Lymphosarcoma	2	....
Adrenal cortical adenoma	2	2.4
Benign	4	4.5
Malignant	84	95.5
Total	88	100

* Pathological classification after operation or autopsy.

TABLE 2.—*Five Year Cures (All Types)*

Type	Number Observed	Survivals	Percentage
Wilms's tumor	30	6	20
Neuroblastoma	15	1	7
Benign: 1 teratoma	1	1	100
Adrenal cortical adenoma	1	1	100
Totals	47	9	19

CLASSIFICATION

The following clinical classification has been found to be generally acceptable:

I. Embryoma of the kidney (Wilms's tumor)
II. Neuroblastoma
III. Benign tumor
IV. Cortical adenoma

A more detailed pathological classification is included in table 1. This indicates the relative frequency of occurrence of the different types.

INCIDENCE AND SEX

Retroperitoneal tumors occurred, on the average, in one in 1,000 patients consecutively admitted to the Childrens Hospital; however, they were responsible for one in 100 deaths. The average age of the patients was 38 months; 53 were boys and 35 were girls (fig. 1).

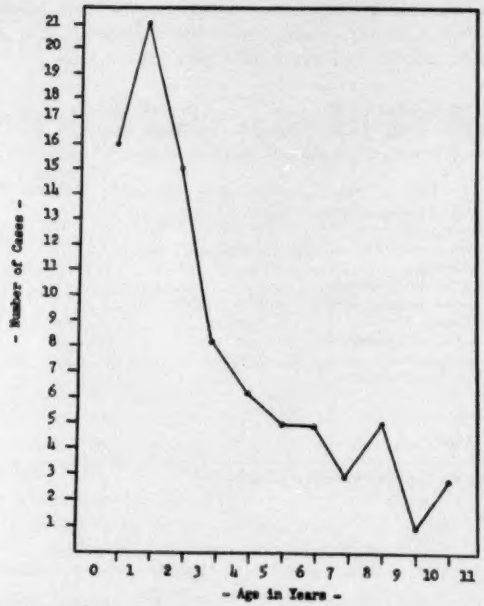

Fig. 1.—The age incidence in 88 cases of retroperitoneal tumor is recorded. The largest number of cases occurred at 1½ years.

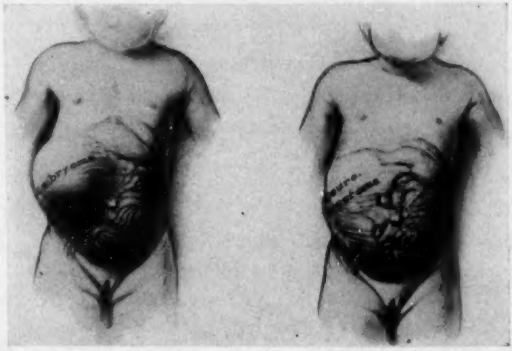

Fig. 2.—Artist's conception of developing retroperitoneal tumor, crowding the intra-abdominal organs.

CLINICAL MANIFESTATIONS

If one visualizes the growing retroperitoneal tumor (fig. 2) as it pushes the posterior peritoneum forward and displaces and crowds the intra-abdominal organs, then one will understand the insidious nature of the onset and the early similarity of symptoms of many of these tumors, regardless of whether they arise from the kidney [2b] or the sympathetic chain [5] or whether they are benign or malignant. There are two exceptions to this simple concept, namely, adrenal cortical adenomas which are readily recognizable by endocrine changes (two examples in this series) and a few of the neuroblastomas [6] which metastasize early, before the primary growth is large (five examples in this series).

The initial manifestation in one half of the children was swelling of the abdomen or palpation of a mass. In the other half, the presenting manifestation had suggested other commoner clinical entities (table 3).

A mass could be palpated in 75 patients after their admission to the hospital, or in 88 per cent of the cases. This, then, is the one characteristic finding, but even this symptom was absent in 12 per cent of the cases. The eleven patients in whom no mass was palpated can be divided into the following groups: (1) children

TABLE 3.—*Predominant Initial Symptoms in 86 Retroperitoneal Tumors (All Types)*

Enlarging abdomen or mass		42-49%
Systemic symptoms		34-39%
Gastrointestinal	19	
Fever or pulmonary	6	
Pain or swelling, not abdominal	7	
Acute abdominal symptoms		10-12%
Appendicitis	3	
Appendical abscess	4	
Ruptured viscus	3	

presenting symptoms of an acute condition in the abdomen (six cases); (2) children with neuroblastomas which metastasized early (five cases). Characteristically, the mass is firm, smooth and nontender, does not move with respiration and is lower than the liver and spleen. During the period of this study, 150 patients with enlargement of the liver or spleen were observed, and the differentiation on clinical grounds alone was often impossible. The assumption that the abdominal mass was a "benign" enlargement of the liver or spleen was responsible for the greatest delay in the admission of children to the hospital. It might be well to point out that in cases of Wilms's tumor the mass is usually smooth, symmetrical and globular, whereas in neuroblastomas, it is often irregular and less distinct in outline. Although these findings are not conclusive, they are often suggestive of the type of tumor.

Systemic symptoms are at times suggestive of the clinical entity produced by a retroperitoneal tumor. Sixty-one per cent of the patients ran an elevated temperature; in the majority of these it did not drop to normal. This finding is evident in the composite temperature chart (fig. 3) but, so far as we are aware, has

5. Wright, J. H.: Neurocytoma or Neuroblastoma, a Kind of Tumor Not Generally Recognized, J. Exper. Med. **12**:556, 1910.

6. Cox, R. A.: Proptosis Due to Neuroblastoma of the Adrenal Cortex (Hutchinson's Syndrome): Report of a Case, Arch. Ophth. **39**:731 (June) 1948. Karsner, H. T.: Distribution of Metastases of Neuroblastoma of Adrenal, Tr. A. Am. Physicians **57**:209, 1942. Aitken, S. G.: Metastatic Neuroblastoma in Bone, New Zealand M. J. **41**:209, 1942.

not been previously emphasized as distinctive. The blood pressure was increased in 46 per cent of the cases in which it was recorded, including 72 per cent of the Wilms tumors [7] and 14 per cent of the neuroblastomas. Urinary symptoms, consisting of pyuria, hematuria or albuminuria, were found in 40 per cent of the cases and were equally distributed between the two major types of tumor.

The one characteristic laboratory finding was an abnormal intravenous or retrograde pyelogram, suggestive of some form of retroperitoneal tumor in 87 per cent of the cases. The usual findings were distortion or displacement of the kidney, pelvis or ureter, suggestive or diagnostic, in 90 per cent of the Wilms tumors and in 75 per cent of the neuroblastomas. The intravenous pyelogram is of especial importance to the surgeon, as it demonstrates function in the opposite kidney.

Roentgenograms of the chest, skull and long bones showed evidence of metastases in 42 per cent of the cases.[8] Predilection of the neuroblastoma for the long bones [9] was demonstrated in 13 cases; however, skeletal involvement also occurred in two of the patients with Wilms's tumor. In one case there was a

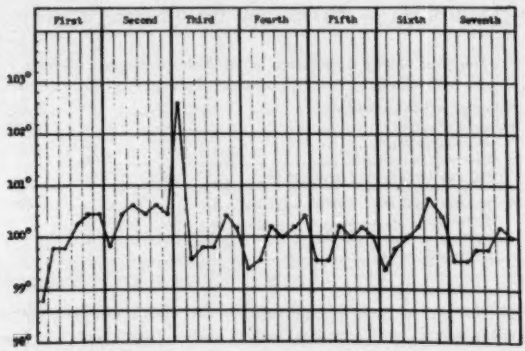

Fig. 3.—Composite temperature chart, prepared by averaging the temperatures as recorded on the charts of 54 patients prior to surgical intervention. The sustained and persistent temperature is manifest.

destructive lesion involving the bones of both wrists, the right radius and ulna, femur and jaw; in the other case only the jaw was involved. This finding is unusual in cases of Wilms's tumor, as recorded in the literature.[10]

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7. (*a*) Bradley, J. E., and Pincoffs, M. C.: Association of Adeno-Myo-Sarcoma of Kidney (Wilms Tumor) with Arterial Hypertension, Ann. Int. Med. **11**:1613, 1938. (*b*) Silver, H. K.: Wilms' Tumor (Embryoma of Kidney), J. Pediat. **31**:643, 1947. (*c*) Hughes, J. G.; Rosenblum, H., and Horn, L. G.: Hypertension in Embryoma (Wilms' Tumor), Pediatrics **3**:201, 1949.

8. Schenck, S. G.: Radiation Therapy for Wilms' Tumor of the Kidney, J. Pediat. **33**: 734, 1948.

9. Willis, R. A.: Metastatic Neuroblastoma in Bone Presenting Ewing Syndrome, with Discussion of "Ewing's Sarcoma," Am. J. Path. **16**:317, 1940. Ackermann, A. J.: Neuroblastoma with Special Reference to Its Roentgen Manifestations, J. Oklahoma M. A. **34**:241, 1941.

10. (*a*) Campbell, M. F.: Pediatric Urology, New York, The Macmillan Company, 1937, p. 260. (*b*) Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941, p. 411. (*c*) Nesbit, R. M., and Adams, F. M.: Wilms' Tumor: Review of 16 Cases, J. Pediat. **29**:295, 1946.

DIFFERENTIAL DIAGNOSIS

The conditions listed in table 4 were initially considered as the tentative diagnosis in 50 of 86 cases.

Blood dyscrasias were a favored diagnosis in 11 cases. Existing blood changes consisting of anemia, variations in the white cell count and a mass on the left side were responsible for this impression. Splenomegaly, aleukemic leukemia and lipoid dyscrasias were considered. Unexplained enlargement of the liver, polycystic kidney, mesenteric cyst and dermoids were frequently mentioned as likely possibilities.

The acute nature of the abdominal symptoms such as nausea, vomiting, abdominal pain and tenderness were sufficiently impressive to result in appendectomy in three cases, and four children were observed for appendical abscess. Recent trauma suggested a diagnosis of ruptured viscus in three cases, with surgical intervention being carried out under this mistaken diagnosis in one.

If, however, one maintains a high degree of suspicion concerning retroperitoneal tumors when an abdominal mass is felt, regardless of the systemic symptoms or the blood findings, and will study a contrast pyelogram, it will be possible to make an early diagnosis in many cases. Roentgenograms of the long bones, skull and

TABLE 4.—*Clinical Entities Confused with Retroperitoneal Tumors in Childrens Hospital Series*

Blood dyscrasias	11
Acute abdomen	10
Splenomegaly	8
Tuberculosis	7
Mesenteric and dermoid cysts	7
Polycystic kidney	4
Orthopedic conditions	3

chest are of importance in the differential diagnosis. Fifteen cases in this series showed evidence of a metastasizing tumor and thus demonstrated the importance of this laboratory finding. In the majority of instances, however, only an exploratory operation will answer the question with certainty.

Up to the present year, only 58 per cent of the cases were referred to this hospital at a stage in which the tumor could be excised. In 42 per cent of these the clinical manifestations were not considered of sufficient importance by the parents and those first seeing the children to warrant hospitalization and definitive treatment.

It is in this large group of cases that a reduction in mortality can be achieved in the future by a more aggressive attitude toward early diagnosis and the use of exploratory laparotomy in those patients with symptoms suggestive of a retroperitoneal tumor.

TREATMENT

Specific curative treatment of a retroperitoneal tumor, regardless of type, requires surgical intervention. If the attending physician and the surgeon can make a presumptive diagnosis early, exploratory laparotomy is indicated to establish the diagnosis and remove the tumor. Also, in all cases in which the tumor is of moderate size, early abdominal exploration and removal appears to be the procedure of choice.

It is in regard to the group of retroperitoneal tumors which have attained really massive size that there is some controversy regarding the advisability of pre-

operative roentgen therapy. Although statistically there is no proof (table 5) that this treatment increases the number of cures, it does diminish the size of the tumor in many cases [11] and thus makes the surgical removal easier. It seems imperative that surgical intervention be delayed no longer than three weeks for the preoperative course of roentgen therapy in order to prevent metastasis.

This form of therapy has been advocated for Wilms's tumor but not for neuroblastoma up to the present time. The safe dose of roentgen therapy has been considered by Wittenborg [8] to be 200 r daily, with a total dosage of about 1,500 r. Furthermore, if the response to such therapy is unfavorable, it need not be continued

TABLE 5.—*Wilms's Tumors in Children*

	All Cases Reported			156 Cases Recorded in the Literature (1941-1950) in Which Nephrectomy Was Done: Statistical Evaluation of X-Ray Therapy; Two or More Years' Survival											
				Nephrectomy Only			With Preoperative X-Ray Therapy			With Postoperative X-Ray Therapy			With Preoperative and Postoperative X-Ray Therapy		
Author	Cases	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead	Total	Alive	Dead
Dean, 1941 *	7	2	5	..	..	..	2	0	2	..	..	..	..	..	..
Morgan, 1943 †	1	0	1	..	..	..	1	0	1	..	..	..	..	..	..
Ockerblad and Carlson, 1943 ‡	1	1	0	..	..	..	..	..	..	1	1	0	..	..	..
Rowe and Frazer, 1944 §	3	2	1	..	..	..	..	..	..	1	0	1	2	2	0
Sugarbaker, 1944 [12a]	1	1	0	..	..	..	..	..	..	1	1	0	..	..	..
Bixler, Stenstrom and Creevy, 1944 ‖	5	2	3	..	..	..	..	..	..	1	1	0	3	1	2
Mellcow, 1944 ¶	9	1	8	1	0	1	..	..	..	..	..	..	4	1	3
Bandler and Roen, 1944 ♯	23	1	22	7	1	6	..	..	..	..	..	..	..	..	..
Mandeville and Nelson, 1945 **	1	1	0	..	..	..	1	1	0	..	..	..	..	..	..
Deming, 1946 ††	3	2	1	2	2	0	..	..	..	..	..	..	..	..	..
Burgess, 1947 ‡‡	1	1	0	..	..	..	..	..	..	1	1	0	..	..	..
Silver, 1947 [7b]	16	9	7	3	2	1	..	..	..	5	3	2	4	4	0
Daw, 1948 §§	7	3	4	..	..	..	..	..	..	3	2	1	2	1	1
Burdick and others, 1948 ‖‖	19	1	18	1	1	0	..	..	..	7	0	7	6	0	6
Schenck, 1948 [8]	17	0	17	..	..	..	..	..	..	8	0	8	4	0	4
Bradley and Drake, 1949 [11]	11	2	9	..	..	..	6	2	4	..	..	..	..	..	..
Dickey and Chandler, 1949 ¶¶	12	4	8	2	0	2	3	2	1	4	1	3	1	0	1
Ritter and Scott, 1949 ♯♯	1	1	0	1	1	0	..	..	..	..	..	..	..	..	..
Gahagan and Yearwood, 1949 ***	14	2	12	1	0	1	2	0	2	5	1	4	4	1	3
Senger, Bell and Barnett, 1950 †††	6	1	5	1	0	1	1	1	0	1	0	1	3	0	3
Neuhauser, 1950 [4]	38	18	20	..	..	..	..	..	..	38	18	20	..	..	..
Totals	212	63	149	24	10	14	19	8	11	79	31	48	34	10	24
Percentage		(29.7)			(41.6)			(42.1)			(39.2)			(29.4)	

* Tr. Am. A. Genito-Urin. Surgeons, **34**: 75, 1941.
† Memphis M. J. **18**: 5, 1943.
‡ J. Urol. **50**: 295, 1943.
§ Radiology **42**: 107, 1944.
‖ Radiology **42**: 329, 1944.
¶ J. Urol. **51**: 333, 1944.
♯ Am. J. Surg. **65**: 306, 1944.
** Urol. & Cutan. Rev. **49**: 204, 1945.
†† J. Urol. **55**: 571, 1946.
‡‡ J. Urol. **58**: 412, 1947.
§§ J. Urol. **60**: 18, 1948.
‖‖ Clin. Proc. Child. Hosp. **5**: 1, 1948.
¶¶ Pediatrics **4**: 197, 1949.
♯♯ J. Pediat. **34**: 753, 1949.
*** J. Urol. **62**: 295, 1949.
††† J. Urol. **63**: 480, 1950.

and operation can be performed without delay. Preoperative roentgen treatment was used in 10 cases in this series.

The fundamental objection to preoperative therapy is the absence of positive proof as to the nature of the mass. It is often impossible to be certain whether one is dealing with a neuroblastoma or a Wilms tumor. Furthermore, benign tumors (two in this series) may masquerade as malignant neoplasms. Splenomegaly hepatomegaly, mesenteric cysts, hydronephrosis, tuberculous kidney (one observed

11. Bradley, J. E., and Drake, M. E.: The Effect of Preoperative Roentgen-Ray Therapy on Arterial Hypertension in Embryoma (Kidney), J. Pediat. **35**:710, 1949.

in this study), appendical abscess (four cases) and ruptured spleen (three cases) may simulate malignant retroperitoneal tumors. In any of these conditions preoperative roentgen therapy would be definitely contraindicated, and one must be wary of its indiscriminate use.

Postoperative roentgenologic therapy, however, has been generally accepted in the treatment of both Wilms's tumor and neuroblastoma. In the latter group of tumors, according to the strong evidence presented by Wittenborg,[8] it is of especial value (table 6). Even though the neuroblastoma cannot be removed in its entirety or even in cases in which intra-abdominal metastases have already taken place, a number of long term survivals have been reported, some of which represent apparent cures (two in this series).

TABLE 6.—*Retroperitoneal Neuroblastoma with Recovery: Cases Reported in Literature with Adequate Verification*

Author	No. of Cases	Age	Surgical Treatment	Irradiation	Known to be Surviving	Metastases at Exploration
Cushing, H., and Wolbach, S. B.: Am. J. Path. 3: 203, 1927	1	11 mo.	Yes	No	15 yr.	No
Wollstein, M.: Surg., Gynec. & Obst. 46: 774, 1928	1	4 mo.	Yes	No	17 mo.	No
Lehman, E. P.: Ann. Surg. 95: 473, 1932	1	11 mo.	Yes	No	15 yr.	No
Goodwin, W. H., cited by Lehman, 1932	1	.....	Yes	...	(No details)	
Wehrbein, H. L.: Am. J. Surg. 45: 332, 1939	2	4 mo.	Yes	No	4 yr. †	No
Cabot Case,[1] 1941	1	4 days	Yes	No	8 yr.	No
Farber, S.: Am. J. Dis. Child. 60: 749, 1940	10	4 days to 8 yr., 11 mo.	....	...	2 to 8 yr.	Yes ‡
Kerley, C. G., in discussion on Farber, 1941	2	9 wk.	Yes	No	4 yr.	No
		2 yr., 3 mo.	Yes	No	12 yr.	To orbit (?)
Bonetti, E., and Scapaticci, R.: Tumori 17: 110, 1943	1	4 mo.	Yes	No	4 yr.	No
Hepler, A. B.: J. Urol. 49: 777, 1943	1	1 day	Yes	Yes	4 yr.	No
Hartz, P. H., and van der Sar, A.: Am. J. Clin. Path. 15: 473, 1945	1	14 mo.	Yes	No	21 mo.	No
Mandeville, F. B.: Urol. & Cutan. Rev. 51: 448, 1947	1	2 yr.	Yes	Preoperative	4 yr.	No
Harrison, F. G., and others: J. Urol. 63: 598, 1950	1	4 mo.	Yes	Yes	22 mo.	Yes
Wittenborg [8] 1950	20	1 day to 13 yr.	Yes: 12	Yes: 12	3 yr. to 16 yr.	6 to liver
Childrens Hospital, Los Angeles, 1950	3	4 mo. to 15 mo.	Yes: 1	Yes: 2	2 yr. to 10 yr.	1 to bone and skin

† Removal seemed incomplete.
‡ Two had local metastases, and two had metastases to liver.

SURGICAL TECHNIQUE

Since in 13 per cent of all cases there was real doubt as to the existence of a retroperitoneal mass and in a larger group there was a reasonable doubt in regard to the nature of the mass, transabdominal exploration seems preferable to the lumbar approach in most cases. Authorities differ [12] in this regard, and no attempt is made to draw any conclusions.

Figure 4 indicates the approach, through a right rectus incision, with the surgeon standing on the right side. The posterior peritoneum has been incised lateral to the ascending colon and the colon and its mesentery retracted to the left side. This method exposes the retroperitoneal structures, as indicated. The same procedure is utilized when a retroperitoneal tumor is present (fig. 5).

12. (*a*) Sugarbaker, E. D.: Application of Staging in Removal of Difficult Wilms' Tumors, Ann. Surg. **120**:901, 1944. (*b*) Ladd and Gross.[16b] (*c*) Nesbit and Adams.[16c]

The next step should be the ligation of the renal vessels if the tumor involves the kidney and if it is resectable. Then the tumor is mobilized, the ureter sectioned and the mass removed. Great caution is necessary in removing the tumor from the overlying lumbar veins and the vena cava.[12a] It is important to include both anterior and posterior layers of Gerota's fascia [12a] with the tumor, as indicated in

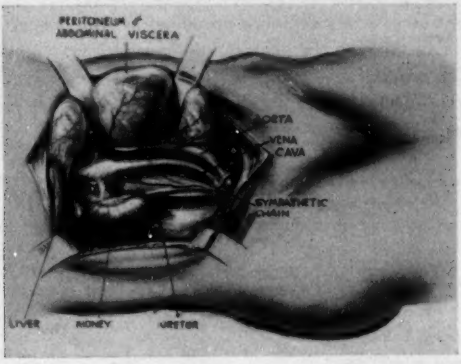

Fig. 4.—Retroperitoneal structures exposed by rotating the ascending colon to the left side.

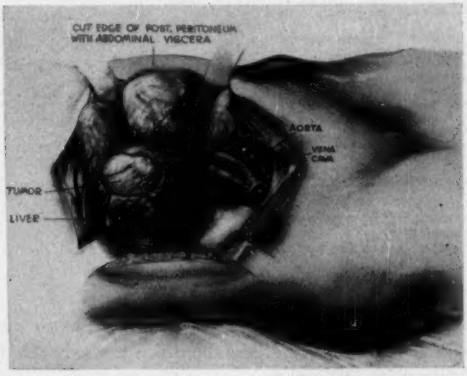

Fig. 5.—The peritoneum has been severed on the lateral aspects of the ascending colon and the retroperitoneal tumor exposed by rotating the colon to the left.

the cross sections (figs. 6 and 7). In the approach for neuroblastomas, the dissection may be much more difficult, but with ample blood a radical attack seems justified in most cases, even if the entire tumor cannot be removed [3] (table 6).

RESULTS

There has been a complete follow-up on all 88 cases of retroperitoneal tumor observed in this hospital. Forty-nine of the cases have now been followed a minimum of five years. The final results in these 49 cases is recorded in table 2. In the series

of 88 cases of retroperitoneal tumors there were two patients with adrenal cortical adenomas. One was well for five years and then had the unusual complication of a Wilms tumor, to which he succumbed a year and a half later. The other patient did not survive. Two of the remaining 86 patients had benign tumors, and these are living and well two and five years, respectively, after surgical excision.

Only 66 of the remaining 84 patients with malignant tumors were treated more than two years ago and can be counted in any final statistical evaluation of results.

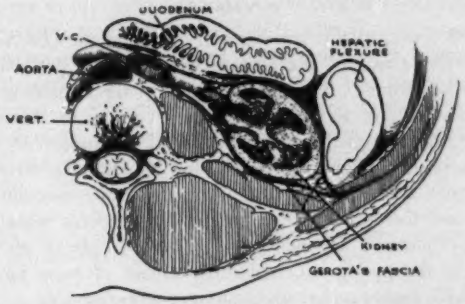

Fig. 6.—The dark line indicates Gerota's fascia, which surrounds the kidney. This is to be included in the resection of the retroperitoneal tumor.

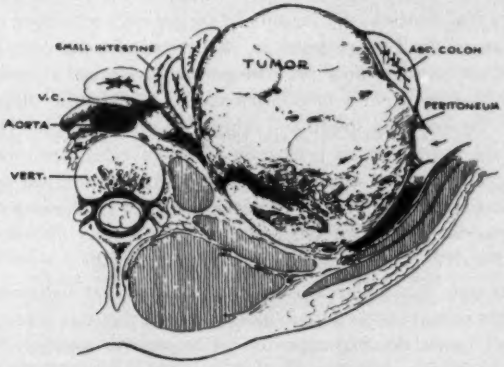

Fig. 7.—Cross section showing the structures overlying the tumor in the retroperitoneal space.

Nine of these patients are living and well, making a two year survival rate for all malignant tumors of 14 per cent. Forty-six children were cared for more than five years ago, and of these 8 are living, making a total five year survival of 17 per cent for the entire group.

One of the patients with Wilms's tumor lived two years and one lived three years, and then both died of metastases. There were 30 children with Wilms's tumor in this group, of whom six are living and well, making a 20 per cent five

year survival rate. This figure is similar to the over-all survival rate tabulated in the literature for 716 cases.[13]

Up to three years ago there were 24 patients with neuroblastomas, and of these three are living and well, a three year survival rate in this group of 12.5 per cent. One of these patients underwent complete excision and received no roentgen therapy; this patient has now survived for 10 years. The other two patients have received roentgen treatment and have now survived for three years.

COMMENT

A survey of 88 consecutive retroperitoneal tumors at the Los Angeles Childrens Hospital is presented; two of the tumors were adrenal cortical adenomas and produced specific symptoms. A large proportion of the remaining 86 tumors produced manifestations as a result of local growth. A few of the neuroblastomas were exceptions to the rule, but on the whole the clinical manifestations were a result of the pressure of a mass extending intra-abdominally from the retroperitoneal area. These manifestations are not peculiar to any one type of tumor but are common to almost all types and therefore make it practical to consider initially all retroperitoneal tumors in childhood as one entity. The presence of an irregular mass, certain changes in the pyelogram, and the presence of bone metastasis help to differentiate Wilms's tumor and neuroblastoma preoperatively.

The initial signs and symptoms in one half of the group were those of an enlarging abdomen and a palpable mass. In the other half systemic manifestations were predominant. These suggested gastrointestinal conditions, blood dyscrasias and other abdominal diseases. By the time of the patient's admission to the hospital, an abdominal mass could be palpated in 88 per cent of the cases. The few in which this was not so were those presenting acute abdominal symptoms and those with diffuse metastases from a neuroblastoma. A differential diagnosis includes enlargement of the liver and spleen and other abdominal tumors. The most clear-cut diagnostic aid was a contrast pyelogram. This revealed a retroperitoneal mass in 87 per cent of the cases. Curative treatment requires surgical excision. This excision was possible in only 58 per cent of the cases and emphasizes the importance of earlier admission to the hospital, roentgenologic studies and early abdominal exploration as the chief future means of improving the results.

From a diagnostic and technical standpoint it is felt that abdominal exploration is indicated as the primary procedure in most cases and that this is best accomplished through a direct transabdominal approach. Preoperative roentgen therapy seems justifiable if the tumor is really massive and strongly suggests Wilms's tumor. In the average case, however, early transabdominal excision of the tumor with postoperative roentgen therapy appears to be the procedure of choice.

The results in this series thus far reveal a 21 per cent five year cure for all types of retroperitoneal tumors. The future, however, looks much brighter if all physicians will keep in mind the clinical syndrome produced by these lesions occupying retroperitoneal space in children and enthusiastically advise prompt hospitalization and treatment.

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13. Harvey, R. M.: Wilms' Tumor: Evaluation of Treatment Methods, Radiology **54**: 689, 1950.

CONCLUSIONS

It is helpful to keep in mind the clinical concept of the symptoms produced by an expanding retroperitoneal mass in infants and children. These are gastrointestinal disturbances, debility, anemia, blood changes, and signs suggestive of acute abdominal conditions. When an abdominal mass is felt, the condition should be considered malignant until proved otherwise. The performance of an intravenous pyelogram is of special importance in the early diagnosis of this condition and in assuring the surgeon that the other kidney is functioning. The recognition that the initial symptoms in one half of the cases will be that of an enlarging abdomen and a palpable mass and that in the other half the initial symptoms will be systemic and consist of gastrointestinal disorders, debility and acute abdominal symptoms will make possible earlier admission to the hospital and increase the opportunity for cures by removal of the tumor. The recognition of the existence of a retroperitoneal tumor is of first importance and its differentiation as to type secondary, although essential for final proper management.

DISCUSSION

DR. GEORGE PACKARD, Denver: Dr. Snyder has covered so interestingly and so thoroughly the subject of retroperitoneal tumors in the young that he leaves me little to say. Our experience at the Children's Hospital in Denver has shown that the great majority of retroperitoneal tumors in this age group are malignant; our end results have not been good. As already stated, with few exceptions these retroperitoneal tumors are either Wilms's tumors or neuroblastomas.

Many of the tumors are actually congenital. Their embryonic nature explains their rapid growth. In comparison with many tumors in adults, they spread like wildfire, either by blood vessel invasion or through lymphatic channels. The disease is acute rather than chronic. Consequently the child, even with a large malignant tumor, often does not have the symptoms of wasting, cachexia, anemia and pain that may attend a malignant tumor in an adult. This fact, I believe, makes the rule that any solid abdominal mass in a child, whether intraperitoneal or retroperitoneal, calls for immediate surgical intervention, but not before preliminary roentgen study for metastasis and helpful localization by urograms as indicated. Time should not be taken for long preoperative study, for repeated manipulation or for preliminary roentgenologic treatment.

We agree absolutely as to the operative approach. It should always be transperitoneal through an adequate incision for the best exposure with the least manipulation. In the case of a Wilms tumor, this approach allows nontraumatic ligation of the pedicle before the growth is handled.

We are heartily in favor of postoperative roentgen therapy and feel that it has been the deciding factor in our few successes. However, I should like to suggest one precaution from our hospital experience. An abdominal neuroblastoma was removed, without the removal of either kidney, and the operation was followed by a course of irradiation. The child died five months later in uremia and without evidence of recurrence of the tumor. There had been no clinical or laboratory evidence of nephritis before the irradiation, and the symptoms and signs of nephritis developed at about the time the irradiation treatment was concluded. Our pathologist, Dr. Palmer, stated that the nephritis was of a unique type. He suspected that it might be the result of irradiation, as it was not unlike lesions produced by irradiation of the kidneys of animals by Dr. Frank Hartman at the Ford Hospital.

On investigation, we found that Dr. Zuelzer, pathologist at the Detroit Children's Hospital, and Dr. Rubin, of the Buffalo Children's Hospital, had had similar experiences after removal of one kidney for embryoma. This feature is worth mentioning, as a growing kidney in a child is apparently more susceptible to irradiation than is the adult kidney. The fact that the kidney is immature and growing is probably more important than that one kidney may be absent. Extra precaution in regard to portal veins has since been taken, without known serious kidney damage.

Our statistical results were not available on short notice. I did select one typical illustrative case. A mass was found in the abdomen of an apparently normal baby, aged 4 months, by a careful pediatrician making a routine physical examination. Retrograde pyelograms showed this typical pattern (slide). A retroperitoneal neuroblastoma was removed transabdominally (slide), and irradiation followed. At 2 years, the baby has shown no evidence of recurrence. I mention this case to show that these tumors are not diagnosed from symptoms but are found, as in this case, by a careful pediatrician (though more often by the mother), that a pyelogram does localize the lesion, that a tumor may be congenital or practically so and that prognosis is not hopeless.

I wish to congratulate the authors on their excellent presentation and to emphasize once more that in this age group practically all these tumors are malignant and require the earliest possible treatment.

DR. E. FELL, Chicago: Two unusual retroperitoneal tumors in the newborn were seen shortly after birth at the Cook County Children's and Presbyterian hospitals.

[Slide]. The reason for showing these is that the patients were operated on three years ago and today both of them are doing very well. The first patient was seen at the Presbyterian Hospital with a low grade obstruction the second day of life. The fluoroscopic view of the colon here shows the sigmoid pushed away to the right side.

[Slide]. At operation, this large retroperitoneal tumor was found and was exposed through a paramedian incision. It was dissected down and was found to be attached to the coccyx. It was a sacrococcygeal tumor. The coccyx and tumor were removed.

[Slide]. This shows the microscopic appearance of the tumor. The little girl, now about 3 years old, is doing well.

[Slide]. The next case was that of a Negro child sent over from the delivery room of Cook County Hospital to the children's surgical service with a diagnosis of imperforate anus and a question of hermaphrodism.

[Slide]. The examination also showed a large tumor in the abdomen, and a Wangensteen test showed that the air bubble was too far above the perineum for a perineal approach.

[Slide]. Through a left paramedian incision, a large tumor presented itself. It filled the abdomen and extended to the xiphoid. Two hundred cubic centimeters of gray, mucoid fluid was withdrawn from the tumor to allow for an easier dissection.

[Slide]. Behind this large cystic tumor we found the blind end of the distal colon. The large retroperitoneal tumor was thought to be a sacrococcygeal tumor at the time of operation. However, it was not attached to the coccyx or sacrum.

[Slide]. It was found that this lesion was a double hydrometrocolpos with a cervix in each cavity. The individual cystic dilatations were about equal in size.

[Slide]. This photomicrograph shows the two cervixes. Detailed study by Dr. George Hass, Pathologist of Presbyterian Hospital, revealed hypertrophy of the secreting glands of the cervix.

As Dr. Packard pointed out, surgical intervention is indicated at times very early in life. In the first case presented cure was accomplished because of early and complete surgical treatment. The second case was considered similar to the first, and not until the tumor was removed was the correct diagnosis made. In retrospect, an abdominal colostomy and drainage of the bilateral hydrometrocolpos through the perineum should have been the procedure of choice.

SPONTANEOUS LATERAL VENTRAL HERNIA

So-Called Spigelian Hernia

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ADRIAN VAN DER SPIGELIUS (1578-1625) was the first to describe the semilunar line. Klinklosch[1] accurately located a hernia in this line. River[2] collected 112 cases from the world's literature and added four cases of his own to bring the total number to 116. Four of these cases had previously appeared in the American literature.[3] Not included in River's review are reports by Miller[4] (one case), Cullen[5] (three cases), Mathews[6] (11 cases), McGlannan[7] (one case) and Sarot[8] (one case). River may have excluded Mathews' 11 cases because the hernias were of the inferior type and are frequently classified as a variety of direct inguinal hernia. Further reports by various authors,[9] and including Mathews' 11 cases, bring

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From the Surgical Service of the New York Medical College, Flower and Fifth Avenue Hospitals, and the Metropolitan Hospital.

1. Klinklosch, cited by Holloway, J.: Ann. Surg. **75**:677-685 (June) 1922.

2. River, L. P.: Spigelian Hernia: Spontaneous Lateral Ventral Hernia Through the Semilunar Line, Ann. Surg. **116**:405-411 (Sept.) 1942.

3. (*a*) Coley, W. B.: Intra-Parietal Hernia at McBurney's Point, Ann. Surg. **1**:246-249, 1909. (*b*) Watson, W. P.: Hernias of the Upper Abdomen, Memphis M. Month. **40**:461-464 (Aug.) 1919. (*c*) Holloway, J.: Spontaneous Lateral Hernias, Ann. Surg. **75**:677-685 (June) 1922. (*d*) Goldberger, H. A., and Panbianco, R. R.: Multiple Hernia, Am. J. Surg. **42**:423-428 (Nov.) 1938.

4. Miller, G. I.: A Correct Definition for Abdominal Hernia Illustrated by 2 Cases: I. Strangulated Hernia Through Linea Semilunaris. II. Intraabdominal Incarcerated Hernia, New York J. Med. **89**:803-204 (April) 1909.

5. Cullen, T. S.: An Extra-Abdominal Multilocular Ovarian Cyst, J. A. M. A. **57**:1251-1255 (Oct. 14) 1911.

6. Mathews, F. S.: Hernia Through the Conjoined Tendon, or Hernia of the Linea Semilunaris, Ann. Surg. **78**:300-304 (Aug.) 1923.

7. McGlannan, A.: Lateral Ventral Hernia, Tr. South. S. A. **39**:162-167, 1927; Ann. Surg. **85**:284-287 (Feb.) 1927.

8. Sarot, I. A.: Hernia in the Linea Semilunaris, J. Mt. Sinai Hosp. **8**:164-166 (Sept.-Oct.) 1941.

9. (*a*) Ebinge, J. B.: Spontaneous Hernia of Linea Semilunaris Spigelii, Nederl. tijdschr. geneesk. **85**:3030-3035 (July 12) 1941. (*b*) Paul, M., and Hill, W. C. O.: Spigelian Hernia with Report on a Case, Brit. J. Surg. **30**:385-387 (April) 1943. (*c*) Caballero, A.: Hernia de

(Footnote continued on next page)

the total number of collected cases to 157, 32 of which appeared in the American literature.

The present report concerns four patients for whom the diagnosis of spontaneous lateral ventral hernia appearing above the inferior epigastric vessels was proved by operation. This report will bring the total number of recorded cases to 161.

The reader is familiar with the standard anatomical definitions and descriptions relating to the structure of the anterior abdominal wall and in particular to the distribution of the fascia and aponeurosis. A remarkable variation in the normal musculoaponeurotic structure of the anterior abdominal wall from the stereotyped textbook descriptions has been recorded (by Zimmerman, Anson, Morgan and McVay [9d] and McVay and Anson [10]). They conclude that the position of the semicircular line is extremely variable and that above the semicircular line there is a marked variation in the composition of the rectus sheath which in most instances conforms to one of the following patterns: (1) division of the aponeurosis of the transversus abdominis at the semicircular line, which then continues medially with gradual decussation of fibers or else ends abruptly to form a secondary semicircular line; (2) the aponeuroses of both the internal oblique and the transversus abdominis muscle divided at the semicircular line to send fibers to both the anterior and the posterior rectus sheath. In addition to the aponeurotic sheath the rectus muscle is enclosed in a fascial sheath (fig. 1).

Further observations by the same authors demonstrated marked variation in the normal anterolateral muscles. The external oblique muscle was the most constant. The internal oblique and transversus abdominis muscles showed considerable variation in the relative amount of muscle and aponeurosis and were often

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Spiegel, Bol. y trab. Soc. argent. cirujanos **5**:232-235 (April) 1944; Rev. Asoc. méd. argent. **58**:448 (June 30), 1944; Día méd. **17**:366-367 (April 23) 1945. (*d*) Zimmerman, L. M.; Anson, B. J.; Morgan, E. H., and McVay, C. B.: Ventral Hernia Due to Normal Banding of the Abdominal Muscles, Surg., Gynec. & Obst. **78**:535-540 (May) 1944. (*e*) Tomaszewski, C. A., and Allende, O. E.: Hernia de Spiegel, Día méd. **17**:1025-1029 (Sept. 10) 1945. (*f*) Capovani, L.: Ernia della linea semilunaris di Spigelio strozzata, Minerva med. **1**:177-179 (April 7-14) 1945. (*g*) Guerreiro, W.: Hernias do sulco do abdomen, Med. cir. farm. **113**: 508-528 (Sept.) 1945. (*h*) Brahm Y, O.: Consideraciones sobre las hernias de Spiegel, Arch. Soc. cirujanos hosp. **16**:388-393 (June) 1946. (*i*) Gonzalez Troncoso, C. A., and Chiesa, C. O.: Hernia de Spiegel estrangulada, Prensa. med. argent. **34**:220-225 (Jan. 31) 1947. (*j*) Bryant, A. L.: Spigelian Hernia, Am. J. Surg. **73**:396-397 (March) 1947. (*k*) Pozzi, G.: Osservazioni sulle ernie ventrali laterali (patogenesi e classificazione), Chirurgia **2**:113-120 (March-April) 1947. (*l*) Sergent, A.: Hernies de Spiegel, Afrique franç. chir. **99**:103 (March-April) 1947. (*m*) Perrigard, G. E.: Superior Semilunaris Hernia Subjacent to Arcuate Line, Canad. M. A. J. **57**:575-576 (Dec.) 1947. (*n*) Chalier, A.: Etranglement de l'appendice dans une hernie de la ligne semi-lunaire de Spigel, Lyon chir. **43**:455-456 (July) 1948. (*o*) Davanzo, G. I.: Sulle ernie spontanee della linea semilunare di Spigelio, Minerva chir. (no. 5) **3**:190-194, 1948. (*p*) Mason, M. L. and Ruge, D.: Spigelian Hernia: Report of a Case, Quart. Bull. Northwestern Univ. M. School **22**:71-73, 1948. (*q*) Watson, L. F.: Hernia, ed 3, St. Louis, C. V. Mosby Company, 1948, pp. 368-372. (*r*) Brosnan, G.: Spigelian Hernia: Report of a Case, M. J. Australia **1**:617-618 (April 16) 1949. (*s*) Reid, D. R. K.: Spigelian Hernia Simulating Acute Appendicitis, Brit. J. Surg. **36**:433-434 (April) 1949. (*t*) Zanaboni, A.: Contributo allo studio della cosi detta ernia di Spigelio, Osp. maggiore, milano **37**:300-303 (July-Aug.) 1949. (*u*) Di Molfetta, N.: Sulle cosidette ernie della linea semilunare di Spigelio, Arch. ital. chir. **71**:103, 1949.

10. McVay, C. B., and Anson, B. J.: Composition of the Rectus Sheath, Anat. Rec. **77**:213-225 (June) 1940.

represented only by fascia or were disposed in the form of musculoaponeurotic bands held together by fascia. Of 100 specimens examined by them, 45 showed a defect in either the internal oblique or the transversus abdominis layer, 10 showed a defect in both layers, and of these 10 the defects were superimposed in 6 instances (fig. 2).

We should like to emphasize the fact that above the umbilicus the fibers of the aponeuroses of the internal oblique and transversus abdominis muscles traverse at

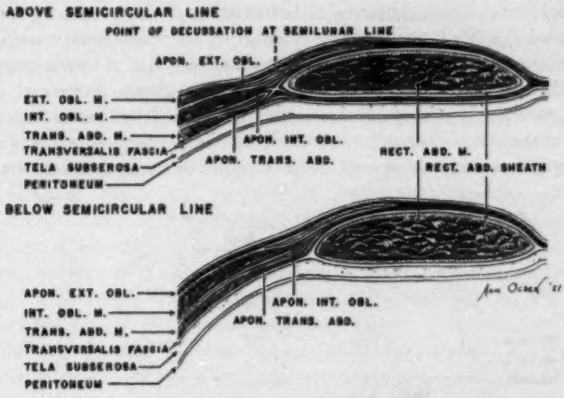

Fig. 1.—Cross section view of the anterior abdominal wall.

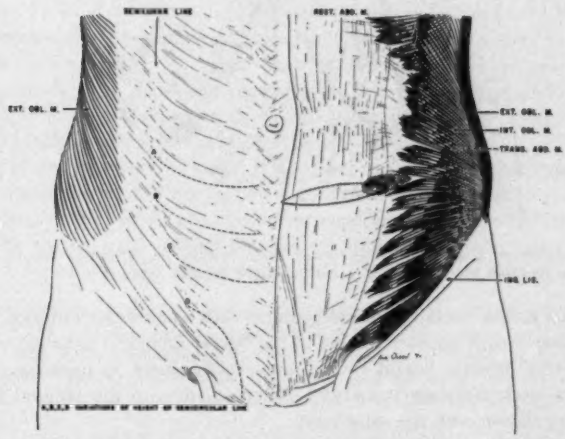

Fig. 2.—Anterior-posterior view of the anterior abdominal wall.

definite angles to each other whereas below the umbilicus they practically parallel each other. This fact may help to explain the relative infrequency of hernia through the linea semilunaris occurring above the umbilicus.

There are two types of spigelian hernias: (1) those appearing above the inferior epigastric vessels and (2) those appearing below the inferior epigastric vessels.

Watson [9q] and Iason [11] agree that most of these hernias appear close to the pubes (the type appearing below the inferior epigastric vessels) and are frequently classified as direct hernia. Recent authors have evaded any attempt to differentiate clearly between direct inguinal hernia and hernia of the linea semilunaris appearing below the inferior epigastric vessels, and perhaps the differentiation is of academic interest without practical applications.

However, both Downes [12] and Mathews [6] did attempt to separate these entities. Mathews preferred the designation of hernia through the conjoined tendon rather than hernia at the linea semilunaris. A study of their accounts reveals well made points that are worthy of reiteration. Spontaneous lateral ventral hernia occurs about equally in males and females and is almost always unilateral. It appears through Hesselbach's triangle between the margins of the rectus muscle and the conjoined tendon or occasionally pushes the conjoined tendon before it. A distinction between direct inguinal hernia and hernia of the linea semilunaris according to

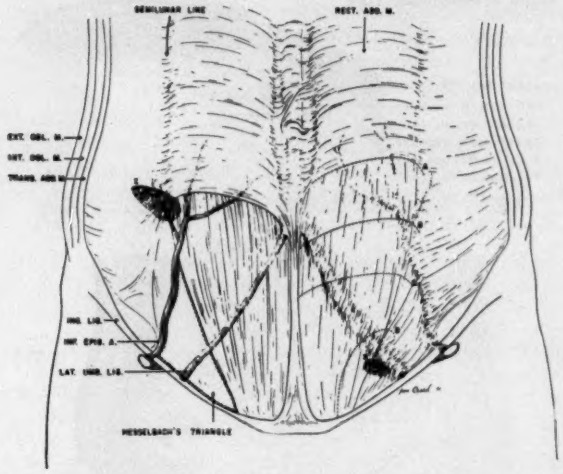

Fig. 3.—Anterior abdominal wall viewed from within the abdomen illustrating at *I* a hernia of the superior type and at *II* a hernia of the inferior type.

their relation to the lateral umbilical ligament fails as an exact criterion. It is true that semilunar hernia appears medial to the lateral umbilical ligament while direct inguinal hernia appears lateral to the umbilical ligament in most cases (fig. 3). The narrow neck with sharp margins resembles that of the femoral hernia and causes strangulation with the same ease.

Stenbuck [13] recently reported one case in detail and mentioned two others which he classified as cases of "direct abdominal hernia." He attempted to differentiate

11. Iason, A. H.: Hernia, Philadelphia, Blakiston Company, 1941, pp. 882-884; Synopsis of Hernia, New York, Grune & Stratton, Inc., 1949, pp. 308-310.

12. Downes, W. A.: Management of Direct Inguinal Hernia, Arch. Surg. **1**:53-73 (July) 1920.

13. Stenbuck, J. B.: Direct Abdominal Hernia, New York J. Med. **48**:2404-2405 (Nov. 1) 1948.

the hernias in these cases from Spigelian hernia; however, we are of the opinion that they are actually Spigelian hernias.

The etiological theories are open to debate. Among the predisposing factors, chronic cough, obesity, pregnancy, ascites and severe muscular effort have been indicted. Sir Ashley Cooper in 1804 was the first to suggest that spontaneous lateral ventral hernia emerges through a vascular hiatus. A number of observers have supported this thesis,[14] whereas others believe it is of minimal etiological significance.[15] Watson [9q] and Iason [11] believe that it is caused by a weakness at the junction of the linea semilunaris with the linea semicircularis, where the posterior rectus sheath is normally absent and there is no fibrous or aponeurotic support between the transversalis fascia and the muscles of the anterior abdominal wall. It should be recalled that Anson and his co-workers [10] showed a marked variation in the structure of the rectus sheath and the anterolateral abdominal muscles, with considerable variation in the amount of muscle and aponeurosis in the internal oblique and transversus muscles, banding of muscle and aponeuroses and a high incidence of musculoaponeurotic defects. We accept this more logical explanation of the etiology of spontaneous lateral ventral hernia. To it may be added the previously mentioned fact that below the level of the umbilicus the muscular and aponeurotic fibers of the internal oblique and transversus abdominis muscles are nearly parallel whereas above this point they traverse at definite angles to each other. This may help to explain the relative infrequency of spontaneous lateral ventral hernia above the umbilicus.

The hernial ring is usually a sharply defined defect penetrating the transversalis fascia, transversus abdominis and internal oblique aponeuroses, situated in or near the linea semilunaris, at its junction with the semicircular fold of Douglas. The orifice is often found at the junction of the medial and middle thirds of a line drawn from the anterior-superior iliac spine to the umbilicus. The ring may vary in size from less than 1 cm. to 8 or 10 cm. in diameter. The peritoneal sac penetrates the transversalis fascia and usually the aponeuroses of the transversus abdominis and internal oblique muscles, to become interstitial lying beneath the external oblique muscle, the so-called masked hernia of Macready. The hernial sac is most frequently single and globular in shape; however, it has been reported as multilocular in form or containing a diverticulum. Frequently, it continues to dissect laterally, appearing most prominent in the region of the anterior superior iliac spine. A large hernia may penetrate the external oblique muscle and appear subcutaneously. Rarely it may lie both subcutaneously and interparietally. Spontaneous bilateral hernias [16]

14. Ferrand, J. A. M. J., cited by Thevenot and Garbourd, cited by River.[2] Thevenot, L., and Gabourd, T.: Les hernies spontanées du repli semi-lunaire de Spiegel, Rev. de chir. **34**: 568-585, 1907. Badoin, R.: Contribution à l'étude des hernies spontanées de la ligne semi-lunaire de Spigel, These de Paris, **2**:269, 1911-1912; cited by River [2] and by Holloway.[3c] Koljubakin, S. Y.: Herniae liniae Spigelii, Arch. klin. Chir. **136**:739-762, 1925. Mason and Ruge.[9p]

15. (*a*) Derycke, P.: Contribution à l'étude de la hernie dite de la zone de Spigel, Bruxelles med. **18**:851-853 (May) 1938. (*b*) Junet, W.: Hernie de la ligne semi-lunaire de Spiegel, Helvet. med. acta **4**:403-406 (Aug.) 1937. (*c*) Lobello, F.: Contributo alla conoscenza dell'ernia spontanea della linea di Spigel, Riforma med. **50**:525-529 (April) 1934. (*d*) Papin, F.: Hernie étranglée de la ligne semi-lunaire de Spiegel, Bordeaux Chir. **7**:203 (April) 1936.

16. Brandtner, C. E.: Über einen Fall von traumatischer Bauchdeckenhernie in der Linea Spigelii, Arch. orthop. u. Unfall-Chir. **33**:219-221, 1933. Berger, P.: Trait. de Chir., ed. 2, Paris, Duplay & Reclus, 1898, vol. 6, pp. 343-348; cited by River.[2] Nyström, G.: Two Cases of Hernia Lineae Spigelii, Acta chir. Scandinav. **56**:92-95, 1923-1924; cited by River.[2]

and sliding hernias [17] have been reported. Frequently the sac is empty at the time of operation. The contents oftenest found are omentum, small intestine or large intestine. In addition, the appendix and ovary have appeared in the sac. Irreducibility, obstruction, strangulation [18] and spontaneous fecal fistula [18b] have occurred.

Symptoms may be absent or the symptomatology obscure and the diagnosis rendered difficult with the small interparietal type, particularly in the obese patient. Nausea, vomiting and persistent or recurring attacks of pain may mimic a variety of gastrointestinal, biliary, renal or pelvic disorders, such as appendicitis, cholelithiasis, intestinal obstruction, ureteral colic and salpingitis. Symptoms may be aggravated by coughing, straining or exertion. If the hernia is irreducible and the cough impulse is absent, it may be extremely difficult or impossible to differentiate from a tumor occurring within the abdominal wall such as lipoma or a fibroma. Three of our patients presented indefinite and ill defined masses that suggested the presence of intraperitoneal tumors, and the correct diagnosis was established only after prolonged investigation which included study of the colon after a barium enema and examination of the genitourinary system by means of cystoscopy and retrograde pyelography. Accurate diagnosis may not be possible until exploratory laparotomy is performed. Lumbar hernia appearing through either the triangle of Petit or the triangle of Grynfeltt and Lesshaft must be excluded. Lumbar hernia appears behind the posterior border of the external oblique muscle. The foregoing comments concerning diagnosis apply to spontaneous lateral ventral hernia occurring above the inferior epigastric vessels. It is impossible to distinguish preoperatively hernia of the linea semilunaris occurring below the inferior epigastric vessels from direct inguinal hernia by either the symptoms or the clinical signs.

Case 1.—H. F., a man aged 74, was admitted to the Flower and Fifth Avenue Hospitals on June 30, 1947. He had been in excellent health until about one year prior to his admission when he suffered an attack of abdominal distention with dull indefinite pain in the left lower quadrant of the abdomen, for which he was treated by his family physician. No mass was noted at that time. His present illness started about 10 days before his admission with the appearance of a tender "lump" in the left lower quadrant of the abdomen associated with a change in his bowel habits. The stools became small in quantity and of decreased caliber. After a barium enema was given his family physician made a tentative diagnosis of tumor of the sigmoid colon and referred him to the hospital for treatment.

Physical examination revealed a fusiform mass about 7.5 by 5 cm. in diameter located in the left lower quadrant of the abdomen adjacent to the anterior-superior iliac spine. It was slightly tender and did not convey an impulse on coughing.

A roentgenogram of the abdomen taken in the dorsal decubitus position showed an indistinct soft tissue shadow in the left lower quadrant lateral to the psoas muscle and well below the left kidney. Examination of the colon by means of a barium enema showed filling of the entire colon without evidence of any obstruction and some spasticity and redundancy of the descending colon and the sigmoid colon, with numerous diverticula. It was suggested that the palpable mass in the left lower quadrant was extracolonic. Examination of the genitourinary tract by means of retrograde pyelography did not show any abnormality. The soft tissue shadow previously observed was not discernible at this examination.

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17. Teale, T. P., cited by Holloway.[3c]

18. (*a*) Massabau, Guibal A., and Cabanac: Deux cas de hernies ventrales latérales spontanées étranglées, Arch. Soc. sc. med. biol. Montpellier **14**:340-350 (July) 1933. (*b*) Scopinaro, A. J.: Hernia de la línea semilunar de Spiegel en un recién nacida, Semana méd. **1**:284-289 (Jan.) 1935. (*c*) Miller.[4] (*d*) Gonzalez Troncoso and Chiesa.[9i] (*e*) Chalier.[9n] (*f*) Papin.[15d]

The day prior to operation, while the patient's abdomen was being examined, it was noted that the mass, which seemed deeply placed and in relation to the sigmoid, assumed a more anterior position on straining and a distinct impulse was noted over it in the abdominal wall. These findings were most distinct with the patient in the erect position. A diagnosis of hernia was made, and it was suggested that this might be a spontaneous lateral ventral hernia. The operation was planned accordingly.

Operation was performed on July 9. The abdomen was entered through a transverse incision in the left lower quadrant. Before the aponeurosis of the external oblique muscle was incised, palpation revealed a small defect in the abdominal wall lateral to the left rectus muscle and slightly below the level of the umbilicus. When the aponeurosis was opened, a hernial sac with a mass of properitoneal fat (4 by 5 cm.) ahead of the sac was found protruding through the defect in the transversus abdominis and internal oblique layers. The ring was about 2.0 cm. in diameter and was above and lateral to the inferior epigastric vessels. The sac was empty at the time of operation. Exploration of the abdominal cavity revealed numerous diverticula along the descending and sigmoid colon; no intraperitoneal tumor or other lesion was noted. The redundant portion of the sac was excised and the hernia repaired.

The postoperative course was uneventful, and the patient was discharged from the hospital on July 18, 1947.

Case 2.—F. H., a man aged 63, was admitted to the Flower and Fifth Avenue Hospitals on Aug. 18, 1947. He had been in good health until the onset of his present illness about seven weeks before his admission to the hospital, when he noted pain in the left lower quadrant of the abdomen. The pain was worse at night time. About one week after its onset he noticed an annoying "lump" in this area. There was no change from his normal bowel habits. The mass gradually became larger. His family physician had entertained the diagnosis of a possible tumor of the bowel or of the left kidney along with a hernia and referred him to the hospital for treatment. A preadmission roentgenogram of the abdomen taken in the dorsal decubitus position suggested a soft tissue shadow in the left lower quadrant of the abdomen.

Physical examination revealed a bulging mass in the left lower quadrant slightly below the level of the umbilicus and lateral to the left rectus muscle, measuring approximately 7.5 by 5 cm., with the long axis in the transverse plane. The mass became larger on coughing or straining and became less apparent when the patient was lying down. It was not tender. A cough impulse was present.

A roentgenogram of the abdomen taken the day after his admission to the hospital failed to show the soft tissue shadow that was present in the preadmission roentgenogram. A study of the colon after a barium enema and intravenous pyelography of the genitourinary tract failed to reveal any abnormality.

A preoperative diagnosis of spontaneous lateral ventral hernia was made. Operation was performed on August 21. A transverse incision was made at the level of the umbilicus from the midline to the lateral border of the left rectus muscle. The aponeurosis of the external oblique muscle was opened transversely and the incision extended medially so as to open the anterior sheath of the left rectus muscle. The rectus muscle was retracted medially. A defect oval in shape and measuring 4 by 5 cm. was found penetrating the transversus abdominis and internal oblique layers in the region of the linea semilunaris. It was above the inferior epigastric vessels. The sac was ovoid and about 6 cm. in its longest diameter. It was opened and the peritoneal cavity entered. Appendices epiploicae presented themselves. Exploration of the peritoneal cavity did not reveal any intraperitoneal lesion, and there was no other defect of the abdominal wall. The closure was made by approximating the peritoneum and the transversalis fascia with interrupted sutures. The transversus abdominis and internal oblique muscles were reapproximated. The anterior sheath of the rectus and the aponeurosis of the external oblique muscle were closed with interrupted sutures. The skin was closed with interrupted sutures.

The patient made an uneventful recovery and was discharged from the hospital on Aug. 29, 1947.

Case 3.—L. R., a white man, aged 54, was admitted to the Metropolitan Hospital on May 19, 1948. Five weeks prior to his admission, the patient first noted a swelling in the right lower quadrant of the abdomen. He sought advice at the clinic because of the swelling and discomfort over this area, which became prominent when he was standing or when he coughed

or strained. The swelling disappeared with the patient lying down. There were occasional attacks of stabbing pain over the mass. Diabetes mellitus had been present for 12 years. The remainder of the history was noncontributory.

On physical examination the abdomen was symmetrical with the patient lying down. However, when his head and shoulders were raised and when he coughed a definite bulging appeared in the right lower quadrant slightly below the umbilicus, extending from the lateral border of the right rectus muscle to the right anterior-superior iliac spine. The defect at the lateral border of the right rectus muscle admitted three fingers. With reduction of the mass and firm pressure along the lateral margin of the right rectus muscle, the bulge was prevented when the patient strained or coughed. A definite cough impulse was noted over this point. The preoperative diagnosis was spontaneous lateral ventral hernia.

Operation was performed on May 21. A transverse incision was made on the right side of the abdomen, extending from the anterior-superior iliac spine to the lateral border of the right rectus muscle. The external oblique aponeurosis was divided transversely. A defect measuring 4 by 5 cm. was found penetrating the transversalis fascia, the transversus abdominis and the internal oblique layer, through which the peritoneum bulged. The defect was superior to the inferior epigastric vessels. The peritoneum was opened and the redundant portion of the sac excised. The sac was empty at the time of operation. The peritoneum and the transversalis fascia were then closed with a continuous suture. The transversus abdominis and the internal oblique layers were closed with interrupted sutures. The external oblique fascia was reapproximated with interrupted sutures. The skin was closed with interrupted sutures.

The postoperative course was uneventful, and the patient was discharged from the hospital on his ninth postoperative day (May 30, 1948).

Case 4.—F. M., a 63 year old Negro woman, was admitted to the Metropolitan Hospital on March 1, 1950, with a history of increasingly severe pain in the right lower quadrant of the abdomen that started four hours prior to her admission. The patient vomited once. She stated that she had occasionally noticed a mass in the right lower quadrant of the abdomen during the past four years but that it always disappeared within a short time. It was present at the time of her admission to the hospital.

Examination of the abdomen showed a large globular mass about 10 cm. in diameter lateral to the right rectus muscle and below the umbilicus. It was hard and tender. A flat plate of the abdomen taken shortly after admission suggested a density in the right lower quadrant of the abdomen. There was no evidence of obstruction. The mass disappeared within two hours of admission, and the patient became asymptomatic. Subsequent examinations failed to reveal any mass or hernial ring even though we searched for a Spigelian hernia. After a barium enema was given the colon appeared normal. The patient was discharged eight days later, to be followed in the Surgical Clinic. On March 21, the mass again became apparent although the patient had no subjective complaints, and she was readmitted to the hospital. The mass could be demonstrated with the patient in the supine position by having her raise her head and shoulders, coughing and straining. Similarly when she was in the erect position, coughing or straining would cause the mass to appear. It appeared lateral to the right rectus muscle, below the umbilicus, was about 6 by 3 by 2 cm., appeared to traverse toward the right anterior-superior iliac spine and transmitted an unmistakable cough impulse.

The preoperative diagnosis was hernia through the Spigelian line. Laparotomy was performed on March 24 through a right lower quadrant oblique incision. The external oblique fascia and muscle were split in the line of their fibers. The internal oblique and transversus abdominis muscles were thin and attenuated. At the lateral border of the right rectus there was a defect through which protruded a hernial sac measuring 3 cm. at its neck and about 9 cm. in length. The inferior deep epigastric vessels were identified and were inferior to the neck of the hernia. The sac was empty at the time of operation. It was opened and the peritoneal cavity entered. Careful exploration failed to reveal any intraperitoneal tumor, and there was no inguinal or femoral hernia present. The redundant portion of the sac was excised, the peritoneum and transversalis fascia closed and repair of the hernia effected.

There was an uneventful postoperative convalescence, and the patient was discharged on March 31 for follow-up in the Surgical Clinic.

SUMMARY

The subject of so-called Spigelian hernia has been reviewed, including the literature, the relevant anatomy and its variations, the etiological factors, the clinical picture and the diagnostic features. We wish to reemphasize the fact that the diagnosis of spontaneous lateral ventral hernia may be difficult to make preoperatively and that frequently it may be confused with a variety of other abdominal lesions, including tumors. Four additional cases have been reported in detail.

DISCUSSION

DR. WILLIS D. GATCH, Indianapolis: A middle-aged man came to me with a reducible swelling just internal to his anterior-superior spine. He had no inguinal or femoral hernia. At operation I found an interstitial hernia which came out through a hole in the transversus and internal oblique muscles. This orifice was an inch and a half (3.8 cm.) in diameter. It was some distance external to the linea semilunaris.

I believe that this hernia was due to a defect in the internal oblique muscle, which I think we all have often noticed in doing a McBurney incision. It consists in a separation, sometimes rather wide, of the fibers of the internal oblique muscle which starts at the anterior-superior spine and extends to the edge of the rectus muscle.

I have not made a study of this subject, as have the essayists, but I believe that in my case, at least, the hernia was due to this defect in the internal oblique muscle.

DR. WALTER L. MERSHEIMER, New York: In answer to Dr. Gatch, it is absolutely true that these hernias emerge adjacent to the semilunar line and then appear to spread laterally to the anterior-superior iliac spine, so that actually the mass is frequently palpated more easily at the anterior-superior spine or adjacent to it than over the Spigelian line.

CHONDROMAS AND CHONDROSARCOMAS OF THE SCAPULA AND THE INNOMINATE BONE

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ROCHESTER, MINN.

THE CHONDROMA in its pure form without any osseous cells may be one of the most troublesome of bone tumors. Because of its cellular nature, its occasional failure to be revealed in roentgenograms and its tendency to extend locally beyond borders which are at best not easily discerned on macroscopic inspection, it becomes a difficult tumor to handle surgically. Add to this the fact that at times some areas of these tumors may be undergoing malignant change while others appear benign and that there is a widespread belief that some of these tumors, apparently benign when first seen, may actually undergo malignant degeneration, and one has an even more serious problem.

Coley [1] made a distinction in chondrosarcomas, classifying some as primary and others as secondary. The latter type "results from a malignant alteration in the cells of a cartilaginous exostosis, a central chondroma or rarely in a patient who has multiple skeletal defects such as a hereditary deforming dyschondroplasia."

Copeland [2] said:

> Secondary chondrosarcoma can be traced in many cases to a pre-existing benign osteochondroma or central chondroma in which repeated removal or trauma (surgical or otherwise) frequently results in a malignant transformation of the cartilaginous tissue. . . . In deciding whether a particular chondroma is to be treated from the benign or malignant standpoint, the location and not the pathologic change is given primary consideration. Lesions in the small bones of the hands and feet may be looked upon as benign and curable by thorough extirpation (curettement and cauterization) . . . when a previously quiescent tumor in the larger bones begins to show signs of increased growth with exacerbation of symptoms secondary malignant change is to be suspected and complete removal is indicated.

At the Mayo Clinic, we have observed several cases in which tumors of this type involved the scapula (fig. 1) and innominate bone (fig. 2). With the collaboration of Meyerding, Mussey and Luckey, I have reported a series of cases of osteochondroma of the pelvic bones.[3] I believe that chondromas and chondro-

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From the Mayo Clinic.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

1. Coley, B. L.: Neoplasms of Bone and Related Conditions: Their Etiology, Pathogenesis, Diagnosis and Treatment, New York, Paul B. Hoeber, Inc., 1949, pp. 282-284.

2. Copeland, M. M.: Cartilaginous Tumors of Bone, American Academy of Orthopaedic Surgeons, Instructional Course Lectures, 1950, vol. 7, pp. 1-18.

3. Ghormley, R. K.; Meyerding, H. W.; Mussey, R. D., Jr., and Luckey, C. A.: Osteochondromata of the Pelvic Bones, J. Bone & Joint Surg. **28**:40-48 (Jan.) 1946.

sarcomas of these two bones at times may be more difficult to diagnose and eradicate than tumors of the same type found in the long bones. Such an impression has been gained from observation of a considerable number of such cases.

Many of these tumors are true osteochondromas with well formed pedicles which can be cut through, and surgical excision can thus be satisfactorily completed. However, that group of chondromas in which one finds pure cartilaginous tissue becomes a much more difficult problem, mainly because of the difficulty one encounters in determining the true extent of the lesion either by roentgenographic examination or by direct inspection of the bone at the time of operation. Such tumors may become rather widespread throughout cancellous bone before they are recognizable in roentgenograms.

The symptoms, too, may vary markedly. Often, when the tumor is small, little is noted in the way of symptoms except mild pain which occurs occasionally. Should the tumor expand in a confined area, pain may become rather steady and at times may be distressing. In other cases, pain is relatively slight or even not

Fig. 1.—Chondrosarcoma, grade 1, of right scapula; *a*, posterior view; *b*, lateral view. This illustration shows the enormous size that chondrosarcomas of the scapula may attain.

noticed until the tumor becomes large enough to be noticeable to the patient either by sight or by palpation. Even then, the roentgenographic picture may not be clear and the bony lesion may be barely noticeable as an area of diminished density on the roentgenogram.

Many surgeons are content with a curettement of the lesion, not being sure that all the tumor is removed. It has been suggested but not proved that surgical intervention without complete removal of the tumor only stimulates the tumor to more rapid growth. This is difficult to prove, but it certainly is my impression, and, as already noted, the same opinion is held by others.

Another possibility is that the tumor may be regarded as a benign chondroma when it actually may be a chondrosarcoma. Such a situation may arise in cases in which microscopic examination discloses chondrosarcoma in parts of the tumor while other parts of the tumor appear benign. The surgeon, in removing a specimen for biopsy, may encounter only benign tissue. Grossly, it is impossible to distinguish benign from malignant tumors.

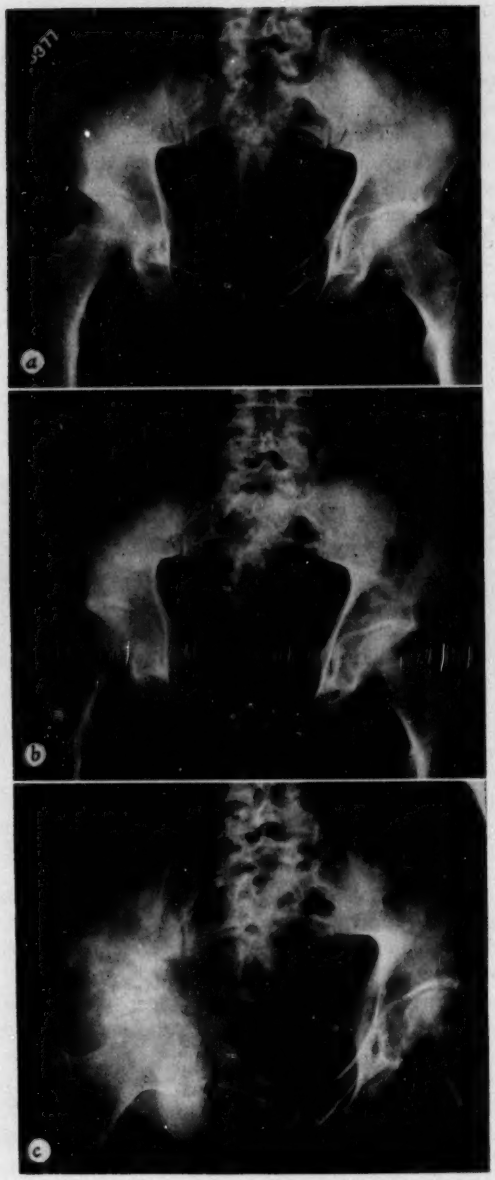

Fig. 2.—Chondrosarcoma of pelvis; *a*, roentgenogram made when patient was first examined at the clinic; *b*, roentgenogram made one year after the one shown in *a*; *c*, roentgenogram made one year after the one in *b*, showing extensive destruction of the right innominate bone. The tumor probably was present when the roentgenograms shown in *a* and *b* were made, although it was not evident in these roentgenograms.

It is my own feeling that although biopsy may be justifiable in cases of this type of tumor the surgeon in planning his operation should contemplate complete extirpation of the tumor at the time of the first operation. When widely and completely removed, the tumor, if benign, will rarely if ever recur. Such removal means a wide resection or, if possible, complete excision of the bone involved. Even amputation may be justified in some such cases although it is admittedly hard to convince the patient of the necessity of such a procedure. However, after one has watched one of these tumors reach its ultimate size, one's conviction about the value of amputation may be strengthened. I have seen four cases in which the tumor was in the late stage of development. The tumors often grow slowly but attain a huge size and cause pain and a prolonged period of morbidity. In cases in which the tumor involves the innominate bone, it is complicated by disturbances in intestinal and vesical function, by lymphatic obstruction with lymphedema of a severe degree, which increases slowly until one wonders how a patient can tolerate such a prolonged and painful illness with only death as the ultimate result.

It has seemed to me that even in cases in which a hind-quarter amputation has been done and the tumor has recurred the terminal stages were less distressing and troublesome than they were in cases in which the tumor has caused a clinical picture such as that described previously. It is such a terminal state as this that has led me to the conviction that treatment of this type of tumor should be early and wide removal of the involved portion of bone, even if this necessitates removal of the entire bone or, in cases of involvement of the innominate bone, hind-quarter amputation. One of my colleagues [4] has succeeded in performing an excision of the entire innominate bone with a good result. Many surgeons have performed scapulectomy, both total and subtotal, and, while total scapulectomy does produce disability with loss of almost all shoulder function, the function of the forearm, hand and elbow remains and the patient is by no means so seriously crippled as he is by an amputation. Such a procedure is much more certain to produce a cure in cases of chondroma or chondrosarcoma than is partial excision or curettement.

I have previously referred to an earlier report on osteochondromas of the pelvic bone. One of my colleagues has recently studied another series of cases [5] of this type of tumor of the innominate bone which were observed at the clinic. In 12 of the 15 cases in which the tumor was a chondroma, the primary operation was performed at the clinic. Follow-up data were obtained in nine of the 12 cases. When the last data were obtained, from two to more than 13 years had elapsed since the operation. All the 9 patients were alive, and there was no evidence of recurrence of the tumor. Twelve cases of chondrosarcoma were studied. In many of these cases, operation had been performed before the patients came to the clinic. Follow-up data were obtained in 11 of the 12 cases. In two of the 11 cases, there was no evidence of recurrence of the tumor when the last follow-up data were obtained. In both of these cases, the patients were treated by a hind-quarter amputation. Follow-up data were obtained for three years after the operation in 10 of the 11 cases. Seven (70 per cent) of the 10 patients were alive more than three years after the operation. Follow-up data were obtained for five years after

4. Lipscomb, P. R.: Personal communication to the author.

5. Starks, W. O.: Neoplasms of the Bony Pelvis, Thesis, University of Minnesota Graduate School, 1949.

operation in eight of the 11 cases. Only one (14 per cent) of the eight patients was living five years after the operation. This patient was treated by a hind-quarter amputation.

It is a well known fact that x-ray therapy has little to offer patients who have chondromas or chondrosarcomas. In fact, it may be stated that it may result in such skin changes as to make adequate operation much more difficult.

Since other types of conservative treatment are of no value, some type of surgical procedure must be performed in order that the patient may obtain the best ultimate result. True, it may at times be difficult to convince a patient of the importance to him of some radical procedure such as those which have been mentioned, and, for this reason, one may be forced to resort to a less extensive resection.

It is my conviction, from observation of cases of chondroma or chondrosarcoma, that the patients should be treated by a radical type of operation even when the lesion is first discovered. Of course, in cases in which wide excision is possible, it may be carried out, but I am convinced that curettement and minimal types of excision should not be done. In the long run, the patient will have been better served by a more extensive procedure. Again, the prolonged morbidity that the patient has to face when the growth progresses beyond surgical intervention leads me to stress this point.

DISCUSSION

Dr. Warner Bump, Rhinelander, Wis.: I thought it might be worth while, because I have seen just a few of these chondromas of the pelvis, to mention how difficult the diagnosis might be. I saw one man with vague symptoms of pain in the hip joint extending down the leg a short distance who was examined thoroughly at several excellent clinics by means of x-rays and even by biopsy and in whom the diagnosis was missed for at least two years. It might be worth mentioning that the diagnosis was finally made by simple rectal examination. Apparently rectal examination for a long time was omitted by all of us who saw him.

Dr. Kellogg Speed, Chicago: I should like to remark that what Dr. Ghormley has shown us covers the field magnificently, and his collection of scapular tumors exceeds anything I have ever seen. The more cellular these tumors are, that is, the more purely cartilaginous, the poorer the prognosis and the faster the growth. On the other hand, the higher the proportion of bone admixed with them, the better is the prognosis.

Pain is the outstanding symptom that the patient will present, and in the early stages even the best roentgenogram may fail to give you a clue to the situation. Consequently, biopsy is absolutely necessary if there is the slightest amount of swelling.

I think it was Phemister who first called our attention to the fact of the slowness of growth of these tumors when he reported three cases, including one of mine and two of his own. I have had one patient, a man, who lived 13 years after a resection of the femur by hip joint dearticulation and finally died with metastases in the lungs and spine.

Dr. Ralph K. Ghormley, Rochester, Minn.: I am glad Dr. Bump emphasized the difficulty in diagnosis in these cases. We have had two other patients similar to the one whose condition he described and the one whose roentgenograms I showed, that is, patients who complained of hip pain. It was impossible to make the diagnosis until the condition as shown in roentgenograms had advanced to the point at which changes were revealed. I say it was "impossible," but on exploration we probably missed the tumor. In one case the lesion finally was found at rectal examination.

What Dr. Speed said about the factor of cellularity of the tumor in worsening the prognosis is true. By the same token, the more cellular the tumor, the more difficult it is to make the diagnosis originally from the roentgenogram.

COVERAGE PROBLEM IN FRACTURES OF THE TIBIA

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DIFFICULT problems of coverage frequently are presented by compound fractures of the tibia. War injuries from missiles make obvious the surface losses from the beginning. After débridement of the wounds and fixation of the extremities, surface coverages were variously effected [1] at a later time, and the plan of attack was generally recognized and standardized. Civilian types of compound injuries of the tibia and adjacent soft parts have caused early and late morbidity. Since large sloughs, osteomyelitis, delayed union, prolonged hospitalization and eventual amputation are frequently seen, a critical review of management seems warranted.

The fracture of the lower part of the leg differs from other fractures. The tibia is a long bone covered over more than one third of its surface with a thin protection of skin, fat and fascia. The skin covering is subjected to frequent trauma but, being distally located, is poorly vascularized. The bone itself shares in the lessened blood supply, much of which comes to it in the chief nutrient artery which enters the bone at the juncture of the upper and middle thirds posteriorly. The hard bone shatters rather than bends, and the detached fragments are devoid of blood supply. Any bone uncovered dies in part. All these facts add to one another to make the tibial compound fracture difficult.

The care of these injuries is chiefly within the province of the orthopedic surgeon. Yet, because of the morbidity cited, the plastic surgeon can be of considerable assistance from the onset in the management of the soft tissue injury and defect. The primary concern should be over the general state of the patient. Shock is common with compound injuries of the extremities and should be prevented by early complete immobilization and treated with blood or its derivatives to maintain the circulating fluid volume. Next in importance is operative reduction and immobilization, but this should not be carried out until the soft tissues are properly cleansed and débrided. There may be massive edema in the soft tissues from

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From the Department of Surgery of the University of Kansas Medical Center.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

1. (*a*) Brown, J. B.: Surface Repair of Compound Injuries, J. Bone & Joint Surg. **26**:448-454 (July) 1944. (*b*) Cannon, B.; Lischer, F. E.; Davis, W. B.; Chasko, S.; Moore, A.; Murray, J. E., and McDowell, A.: The Use of Open Jump Flaps in Lower Extremity Repairs, Plast. & Reconstruct. Surg. **2**:336-341 (July) 1947. (*c*) Edwards, S.: Evaluation of the Open Jump Flap for Lower Extremity Soft Tissue Repair, Ann. Surg. **128**:1131-1135 (Dec.) 1948. (*d*) Soderberg, B. N.: Massive Combined Tube and Open Flap Used as Unity Rotation Pedicle Transplant for Repairs of Certain Deep Surface Defects, Plast. & Reconstruct. Surg. **3**:407-416 (July) 1948.

the primary injury or more likely from the motion of the jagged bone ends poorly immobilized. The greater the swelling the less the chance for local survival of the soft parts.

Local wound care is accomplished in the most careful manner, clothes being cut away, gross dirt removed with bland soap and water, hair shaved, grease dissolved with a solvent, usually ether or benzin, and the wound flushed with copious quantities of saline. After redraping, wound débridement is carried out, which includes trimming away irregular blue skin edges, nonviable fat and frayed fascia, cutting out brown, gray or blue muscle which does not contract when stroked, removing only bone detached from its periosteum totally and flushing out blood clots and debris. Bleeding points should be ligated with care. With the wound cleansed and relatively dried, the fracture can be reduced in the best fashion possible, and then, and not until then, wound closure is contemplated.

The surgeon of trauma must exercise considerable judgment. Time should not be wasted, as the patient is a candidate for shock; yet great hurry is not indicated in wound care, especially if blood is available. Wounds observed late, usually after eight hours, already will show signs of inflammation and should not be closed but treated openly and closed secondarily a few days later. If the wound is closed and uninfected, the healing time and bony union likely will proceed as with a simple fracture, but if the soft tissues slough, all or any of the undesirable complications may occur.

There apparently have been attempts made forcibly to obtain closure, edematous devitalized skin margins being pulled together with coarse suture material. Such attempts have failed many times. Relaxing incisions along the sides have permitted successful closure in many cases. Rotation or interpolated flaps have rarely been tried, and almost never has tissue been brought from a distance, primarily. An immediate cross leg flap by Gissane [2] was successful, permitting the fracture to heal promptly.

The cross leg flap, providing the opposite leg is available, is the best means of coverage if tissue from a distance is needed. The calf is the usual donor site and can be used for a direct transfer with a high percentage of success if proper attention is given to principle and detail.[3] The flap should have a base as wide as possible, best at least as wide as the flap is long. The base should be proximal, the direction of the inflow of blood. There should be a minimum of rotation, kinking or stretching of the raised flap. A skin graft should be sutured to the donor bed. A plaster cast must be correctly applied and rigidly maintained with the leg in proper position.[4] This is the hardest and most important part of the operation. The position of the legs may not be the best for proper bone alignment, but a little

2. Gissane, W.: Thoughts on the Clinical Organization of a Regional Accident Service, Brit. J. Plast. Surg. **2**:224-232 (Jan.) 1950.

3. (*a*) Converse, J. M.: Plastic Repair of Extremities by Non-Tubulated Pedicle Skin Flaps, J. Bone & Joint Surg. **30A**:163-194 (Jan.) 1948. (*b*) Jayes, P. H.: Cross-Leg Flaps: A Review of 60 Cases, Brit. J. Plast. Surg. **3**:1-5 (April) 1950. (*c*) Lewin, M. L.: Resurfacing Procedures in Compound Injuries of Lower Extremities, Ann Surg. **128**:66-79 (July) 1948. (*d*) Padgett, E. C., and Gaskins, J. H.: Use of Skin Flaps in Repair of Scarred or Ulcerated Defects over Bone and Tendons, Surgery **18**: 287-298 (Sept.) 1945.

4. Robinson, D. W.: The Coverage Problem of the Injured Extremity, South. Surgeon **16**:933-953 (Oct.) 1950.

angulation can be corrected while the callus is still soft at three weeks, the usual time of detachment of the legs and removal of the cast. Surface healing is here more important than a straight bone. Without a good coverage, bony healing rarely takes place.

Revision or resetting of the free redundant margin of the flap can be accomplished in a few weeks after detachment of the legs. Too early a revision often causes infection or local loss of tissue.[4] Within a month or two the flap can be used to operate through as is necessary. Often, though, bony union takes place well when there is good surface coverage, making unneeded the bone graft thought to be necessary.

The management of the late cases with exposed bone and much peripheral scarring differs only in that it is necessary to remove the bone back to a region of good bleeding and to remove the scar to good viable tissue before suturing down a flap. Osteomyelitis must be controlled and chronic dermatitis should be cleared up. Frequently a nonunion which has lasted for many months heals when good coverage has been added. It is sometimes wiser to clear out the dead bone and infected granulation tissue. After saucerization, a few days of pressure wet dressings changed at least once daily will produce fine healthy granulations on which a thin split graft will take. The dirty wound is made clean. A flap can be shifted more successfully later with less infection from "tenting" or "pocketing," as would occur often with early direct flap coverage. With these more elective cases, the direct flap can be used, but for greater insurance of success and for better positioning of the legs, a flap of a design not directly in line with the blood supply can be used providing it has been raised and delayed. Retrograde or hinged flaps can be used in this manner.

Selection of the type of flap and the manner of its execution may be altered by judgment in relation to the age of the patient, vascularization of the leg, status of the opposite leg, degree of obesity and general well-being. The patient over 60 years tolerates a cross leg cast poorly and, if abnormal flexion is needed, may have a relatively stiff knee when the cast is removed. The arteriosclerotic patient is not a good candidate for a flap as his local tissues may be avascular, making flap viability poor and threatening pressure sores. Casts should be well padded with sheet wadding and felt over bony prominences. A Balkan frame over the bed helps to suspend the weight of the cast by means of ropes and pulleys. A monkey bar makes more easy the use of the bed pan.

Local flap shifts from the margins are sometimes useful. Often, the injury from the beginning makes doubtful the viability of the local tissues, which rarely can be transferred in one stage. Two or three elevations of the flap in stages give more insurance of success. Lack of availability of the opposite leg makes necessary the local tissue transfers. The first stage consists of undermining between parallel incisions in normal healthy tissue. After 10 to 16 days, the distal end of this flap can be cut and resutured. When edema has been resolved, the flap can be raised and rotated, a free skin graft being applied to the donor flap site. If there is doubt about the vascularity of the flap when it is sectioned and made ready for transfer, it should be returned to its bed and used a few days later.

Amputation, the last resort, may finally be necessary. One can easily cut off a limb but one finds salvage or reconstruction much more difficult. There are definite

times, however, when early amputation is sound judgment. Surface-covering operations may require much time but when completed may not make the extremity useful because of osteomyelitis, nonunion or absence of bone for continuity or weight bearing. Before amputation is definitely decided on, the transfer of tissue from a distance, such as carrying an abdominal flap on the forearm [5] or wrist, should be considered in regard to the probable end result and the feasibility and practicability of its accomplishment.

REPORT OF CASES

CASE 1.—J. D., a white man aged 27, at the age of 5 years had been burned on the right shin. The skin healed gradually by scarring but gave him no trouble. On the day of his admission to the hospital, March 14, 1948, while he was carrying a piano upstairs, his leg snapped

Fig. 1 (case 1).—*A*, defect of skin in old burn scar with tibial fracture ends showing. Scar to be replaced by a suitable flap for healing. *B*, flap margin just after suture removed from revised edges. Skin graft in donor bed of lateral hinged cross leg flap.

under him and the bones were exposed by a break through the scar. The orthopedist put him in a cast and tried to close the wound through the scar. The repair broke down, so that the plastic service was asked to see him several days later (fig. 1 *A*). On March 29 a flap on the opposite calf was raised and resutured in its bed. In two weeks the cross leg flap was attached. It was detached three weeks later and revised three months later (fig. 1 *B*), union having taken place in osteoporotic bone under an old burn scar. The patient was at work in three months after the revision.

CASE 2.—E. B., a 45 year old white man, in late June 1949 suffered a compound fracture of his left tibia, with considerable gross contamination and local tissue damage. Attempted

5. Cannon and others.[1b] Jayes.[2b] Soderberg.[1d]

closure of the wound by the orthopedist was unsuccessful (fig. 2*A*). He was first seen by the plastic service in July when I raised a lateral flap. This was not transferred for about seven weeks (fig. 2*B*). The result was such that although much dead bone was present union of the fracture took place over the next four months, negating the bone graft at first thought necessary.

CASE 3.—A. S., a 24 year old white woman, as the result of an automobile accident had her right leg amputated above the knee and the left lower leg fractured in several places, the tibia compounded near the ankle. Attempted closure early had produced a slough (fig. 3*A*). Local tissue had to be used as the other leg was not present and a prolonged transfer of tissue carried by the arm was not desired. A large flap was outlined on the adjacent anteromedial skin (fig. 3*B* and *C*). Two longitudinal parallel incisions were made first and the soft tissues between under-

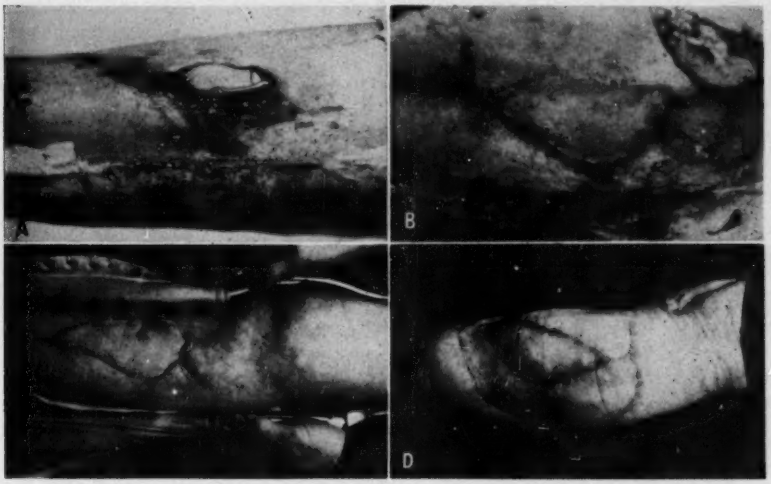

Fig. 2 (case 2).—*A*, defect of shin six weeks after compound fracture. Note bare bone and metal plate showing. *B*, hinged lateral cross leg flap in place 10 days after attachment, sutures just out. The dead bone and plate had been removed. *C*, flap in place six months after detachment (revision one month later), union definite and, in spite of considerable bone loss, no bone graft needed. The brace is for support only. *D*, donor calf with skin graft showing the extent of the flap nine months after operation.

mined completely over the muscle fascia. Two weeks later the lower end was sectioned and sutured as another delay. The third stage, two weeks after the second, raised and rotated the flap after the dead bone and granulation tissue had been removed. A split skin graft closed the donor bed (fig. 3*D* and *E*). Healing was per primam (fig. 3*F*). Bony union took place within four months, but a sliding bone graft had to be done for a tibial nonunion near the tubercle. The leg was salvaged and will allow her much greater mobility than if it also had been removed.

CASE 4.—This was a Veterans Administration case involving a 65 year old white man. Eight weeks before he was seen by the plastic surgery service he had received a severe compound fracture of his right lower leg. There was a considerable slough of the skin (fig. 4), with much bone exposed. After deliberation, it was decided not to do flap coverage but to try saucerization and skin grafting or amputation. It is felt that this man will be rehabilitated the most completely and quickly by an amputation in view of his age, the stiffening of his joints from a crossleg cast, the length of hospitalization and the possible complications following flap coverage and subsequent bone grafts.

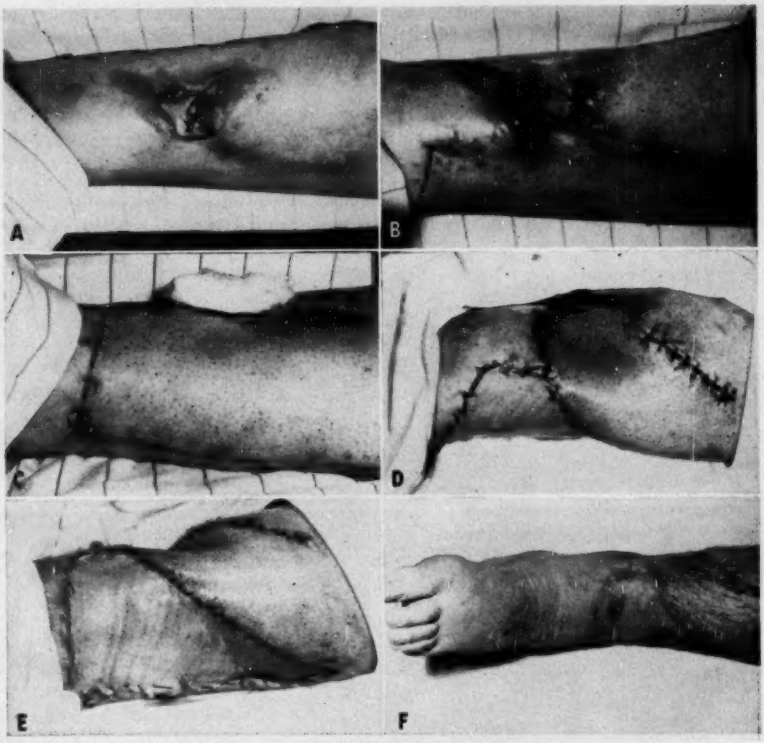

Fig. 3 (case 3).—*A*, defect of skin two months after injury which required amputation of other leg in lower part of thigh. *B*, lower end of delayed lateral flap showing sutures still in place after section of lower end of flap, as second stage of procedure 18 days after first. *C*, extent of raised flap. First stage was undermining to muscle fascia between the healed parallel incisions. Gauze is over exposed bone. *D*, at third stage (four weeks after first stage) flap rotated over defect, following careful removal by saucerization of dead bone and old granulation tissue. A split skin graft covers the donor bed defect. *E*, extent of donor bed with covering skin graft. *F*, leg four months after flap rotation. There is good bony union beneath the flap. Nonunion at another fracture site near tibial tubercle required sliding bone graft.

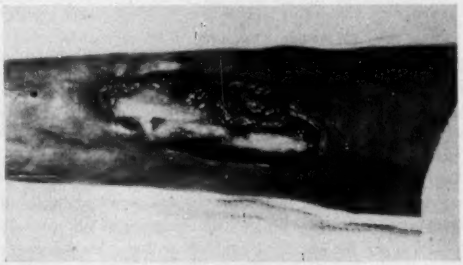

Fig. 4 (case 4).—Large defect of skin with considerable exposed tibia and peripheral scarring. Because of age (65 years), probability of length of procedure and possible poor outcome, amputation was considered.

CASE 5.—The patient, a 32 year old Negro, had both legs severely fractured three weeks before he was seen by the plastic surgery service. The right leg showed a huge defect of soft tissue over the exposed, detached, comminuted bony pieces (fig. 5). Amputation was considered but outvoted, chiefly because of the patient's young age and outlook. The dead bone was removed in four weeks, and by means of daily changes of wet pressure dressings with fine meshed gauze next to the wound suitable granulations were produced. A thin split skin graft took well in the saucerized cavity. Before shifting of a flap to permit subsequent bone grafting, the patient signed his release and has not been heard from since.

CONCLUSIONS

1. Compound fractures of the tibia often present a special problem of coverage.

2. Gentle handling of tissues is mandatory to prevent sloughing, with all its following bad complications.

3. Sliding or rotation flaps are possible with minimum soft tissue damage, but it is urged that cross leg flaps for primary closure be tried if there is much damage.

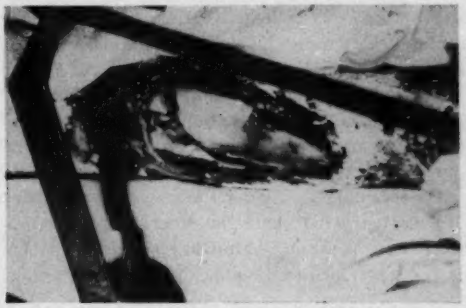

Fig. 5 (case 5).—Large slough over tibia with much exposed comminuted bone; other leg severely fractured (three weeks after injury). Dead bone was removed and a successful skin graft closed the saucerized clean cavity, but the patient signed a release.

4. Dead bone and infected old granulation tissue have to be cleaned up before late coverage is tried. A skin graft will give early coverage to a properly prepared saucerized wound, making clean a dirty wound.

5. A flap is needed to operate through for a bone grafting procedure, but a good viable flap may produce union in a long-standing ununited tibial fracture.

6. Occasionally amputation is the quickest and best solution for the severely infected, open, ununited fracture.

DISCUSSION

DR. RALPH G. CAROTHERS, Cincinnati: I should like to point out that most of these cases involve bumper fractures, and there are occasions when the skin looks good. The fracture may not even be compounded, but there has been a period of a moment or so in which the skin and overlying flesh have been severely crushed between the bumper of the car and the tibia before the latter broke. Therefore, even in a simple fracture this same problem can arise at a later date.

The answer to it, of course, is to have the leg so splinted that the skin can be observed right along. I think that relaxing incisions can be so placed and immediately closed with split thickness grafts that in the majority of cases closure can be done safely.

EFFICACY OF HEMOSTATIC AGENTS IN THE PRESENCE OF ANTICOAGULANT THERAPY

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FREDERICK W. PRESTON, M.D.
AND
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IN CERTAIN circumstances it may be desirable to perform some types of vascular surgery while the patient is under the influence of anticoagulant therapy without first neutralizing the anticoagulant effect throughout the body. This situation holds particularly in the surgery of arterial embolism. Advantages appear to be (1) prevention of propagation of the embolus preoperatively and during operative manipulation, (2) prevention of formation of a new thrombus at the freshly sutured site of arteriotomy, (3) obviation of the difficulties and hazards of regional postoperative heparinization and (4) control of all bleeding at the operating table while the patient is under the influence of heparin to prevent formation of wound hematomas which might otherwise develop if heparin therapy were instituted only after operation. Laufman and Heller [1] in 1943 showed that if a hematoma does not develop in a wound, anticoagulants will not interfere with wound healing.

Among those who prefer to perform vascular surgery during heparin therapy are Murray,[2] Lindgren and Wilander [3] and Schumacker and Abramson.[4]

Recently, while performing an operation for the removal of a femoral embolus on a heparinized patient, one of us (H. L.) found it necessary to transect a large mat of chronically inflamed inguinal lymph glands. The oozing surfaces were readily controlled with gelatin sponge, and the embolectomy was performed without incident. Subsequently, gelatin sponge was used in operative wounds in three

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Technical assistance was given by Alfred Ross, M.D.

From the Department of Surgery, Northwestern University Medical School.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

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2. Murray, G.: Heparin in Thrombosis and Blood Vessel Surgery, Surg., Gynec. & Obst. **72**:340-344, 1943.

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additional embolectomies, all performed during heparinization. The sutured arteriotomy incisions remained dry in every case without the aid of hemostatic agents. The gelatin sponge was left in place in three of the cases, and the operative wounds were closed with widely spaced interrupted sutures. In no instance was there any interference with wound healing. In one case the gelatin sponge was removed before closure of the wound. This patient's dressings were blood-soaked

Fig. 1.—Low power photomicrograph of dog spleen showing appearance of gelatin sponge in wound. This animal was in the control series and received no anticoagulant therapy.

the next morning. On removal of the dressings, a trickle of blood was noted from the lowermost angle of the wound. A small amount of gelatin sponge was packed into this area, and no further bleeding occurred. It was not necessary in any of these cases to neutralize the general anticoagulant effect at any time until purposeful discontinuance of therapy after seven days.

The local control of bleeding during surgical procedures on a heparinized patient has been accomplished heretofore with fibrin foam by Schumacker.[4]

In order to establish the value of gelatin sponge as a hemostatic agent in the presence of anticoagulant therapy, we undertook a controlled experiment on dogs. To make the test more critical we used the spleen as the test organ. Such a parenchymatous organ would be expected to bleed more freely than would skeletal tissues. We wished to determine to what extent one could depend on gelatin sponge during surgery and whether temporary control would give way to late bleeding if the subject were maintained on anticoagulant therapy.

METHODS

Twenty-three fasting mongrel dogs, male and female, were operated on under intravenous pentobarbital (nembutal®) anesthesia after preoperative studies were made on the blood. These studies consisted of determination of prothrombin activity, coagulation time, hematocrit and sedimentation rate. The spleen was exteriorized through a midline abdominal incision. Four to ten rectangular segments, each measuring 1.5 by 0.25 by 0.25 cm., were removed from the anterior central portion of the spleen. These wounds were managed as follows. Three types of control consisted of (*a*) permitting a wound to bleed freely, (*b*) packing a wound with frayed cotton covered with a cotton plaque and (*c*) packing with coarse mesh gauze.

The test wounds were treated by packing the wound completely with gelatin sponge and covering with a gelatin sponge plaque (fig. 1).

We found that the usual type of digital pressure, which is sufficient to control bleeding when gelatin sponge is used, consists of about 40 to 50 Gm. as determined by the use of metal weights. Therefore, in the majority of experiments ordinary digital pressure was applied to the various types of packing described after the amount of pressure was determined by the metal weights.

Anticoagulants were administered in the following four ways: 1. Aqueous heparin was given immediately prior to and during surgery. 2. Dicumarol® was given 48 to 96 hours preoperatively and for five days postoperatively. 3. Aqueous heparin was given immediately prior to surgery and repository heparin postoperatively for five to seven days. 4. Repository heparin or aqueous heparin and dicumarol® was given two and a half to six hours preoperatively and dicumarol® for seven days postoperatively.

Careful checks were made on coagulation time by the Lee-White method, while prothrombin activities were determined by the one stage method of Quick and expressed in per cent of prothrombin activity. In several instances recognized safe clinical levels were deliberately surpassed in order to produce a most rigid test. Since we found that variations in the coagulation time within a given postoperative day permitted an occasional instance of escape to nontherapeutic levels, the coagulation times were determined three times daily, at 8 a. m., 4 p. m. and 11 p. m. We consider therapeutic yet safe levels of prothrombin activity to range between 10 and 30 per cent and those of coagulation time between 15 and 30 minutes.

RESULTS

Aqueous Heparin Preoperatively and During Operation.—Gelatin sponge effectively controlled splenic bleeding at the time of operation in each of two dogs treated. The coagulation time of the first animal was 20 minutes at the time of operation. There were no deleterious after-effects. The studies on these two animals were considered as pilot experiments since no postoperative treatment was to be instituted. Consequently, the coagulation time of the second dog was increased to 180 minutes at the time of operation. Although bleeding was controlled at operation by the gelatin sponge, late bleeding occurred and this animal was found dead from hemorrhage in his cage the next day.

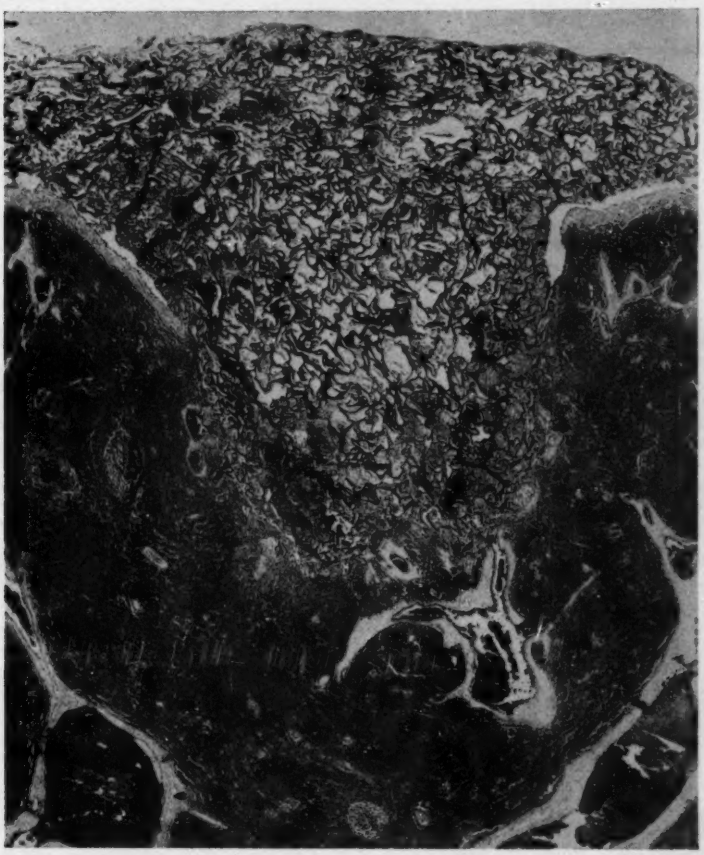

Fig. 2.—Low power photomicrograph showing gelatin sponge in splenic wound of dog D8. Animal received dicumarol® preoperatively and postoperatively. Gelatin sponge successfully controlled bleeding. The specimen was removed seven days postoperatively.

TABLE 1.—*Efficacy of Gelatin Sponge in Splenic Wounds with Dicumarol® Preoperatively and Postoperatively*

Animal No.	Prothrombin Activity at Operation, %	Postoperative Range of Prothrombin Activity, %	Days Observed	Comment
D2	2.7	<1	4	Died 4th postoperative day; no blood in abdomen at autopsy; some external wound bleeding
D3	13.4	<1	3	Gross blood in bowel and lungs; none in abdomen; external wound bleeding; died 3d postoperative day
D4	9.7	<1.7	2	Abdomen filled with blood from splenic wound; died 2d postoperative day
D5	14.9	4.5 to 19	9	Escape to 60%, one reading 4th postoperative day; killed; clean peritoneum
D6	20.4	4.5 to 18.5	6	Killed; clean peritoneum
D7	11.5	3.3 to 22.5	7	Killed; clean peritoneum
D8	18	16.4 to 28	5	Killed; clean peritoneum

TABLE 2.—*Efficacy of Gelatin Sponge in Splenic Wounds with Repository Heparin Preoperatively and Postoperatively*

Animal No.	Coagulation Time at Operation, Min.	Postoperative Range of Coagulation Time, Min.	Days Observed	Comment
DH1	33	10 to 35.0	9	Killed
DH2	30	10 to 60	9	Killed
DH3	90	90	2	Died of external bleeding
DH4 *	25	10 to 50	8	Killed
DH5 *	45	10 to 50	7	No ill effects; killed; hematoma (3.5 × 2.5 cm.) of spleen

* Aqueous heparin preoperatively, repository heparin postoperatively.

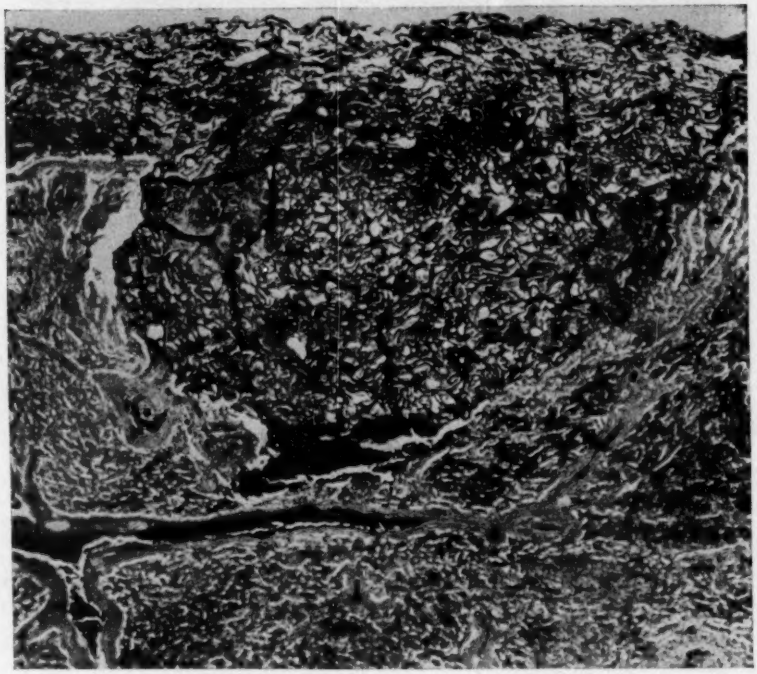

Fig. 3.—Low power photomicrograph showing gelatin sponge in splenic wound of dog DH3 24 hours postoperatively. This dog received repository heparin which produced a coagulation time of 90 minutes. The animal died of external bleeding from the abdominal incision, but the splenic wound remained dry.

Dicumarol® Preoperatively and Postoperatively (Table 1).—Gelatin sponge effectively controlled the splenic bleeding at the time of the surgical procedure in each of seven dogs given dicumarol® with prothrombin activity ranges from 2.7 to 20.4% (Fig. 2). In one dog the prothrombin activity at the time of the operation was 9.7 per cent and gelatin sponge controlled the bleeding effectively. However, the next morning the prothrombin activity dropped to 1.7%, and this animal bled to death from both the splenic wound and the abdominal wound later that day.

It was interesting that this dog had bleeding gums at the time of operation although his prothrombin activity at that time was practically within a safe therapeutic range. Two other animals whose prothrombin activities dropped to under 1% had no postoperative bleeding from the splenic wounds, although they bled from other areas.

Aqueous Heparin Preoperatively and Repository Heparin Postoperatively for Five to Seven Days (Table 2).—In five animals treated, gelatin sponge effectively

Fig. 4.—Low power photomicrograph showing appearance of gelatin sponge in splenic wound of dog DH4 eight days postoperatively. This dog received aqueous heparin preoperatively and repository heparin postoperatively for eight days. The empty space represents an area of gelatin sponge which was intact at the time the specimen was taken but which was lost in the fixing solutions. However, note that the rim of the wound is well coagulated by the gelatin sponge.

controlled the splenic bleeding at the time of operation as well as postoperatively (Figs. 3 and 4). We found that the absorption from repository heparin was highly irregular, and it was difficult to prevent greatly prolonged coagulation times in some instances and temporary escapes from therapeutic levels in others. In one

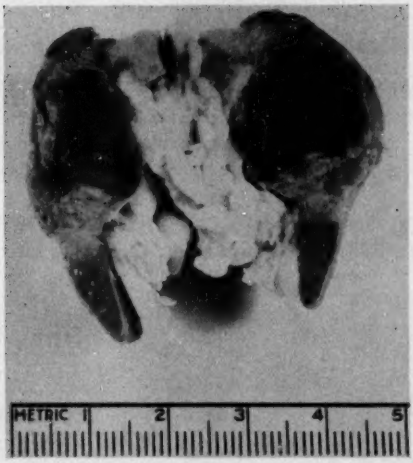

Fig. 5.—Gross appearance of spleen removed after seven days from dog DH5. This dog received aqueous heparin preoperatively and repository heparin postoperatively. There were no ill effects despite the large hematoma within the spleen. The gelatin sponge was apparently not packed to the bottom of the splenic wound, which allowed the hematoma to form. There was no bleeding into the peritoneal cavity.

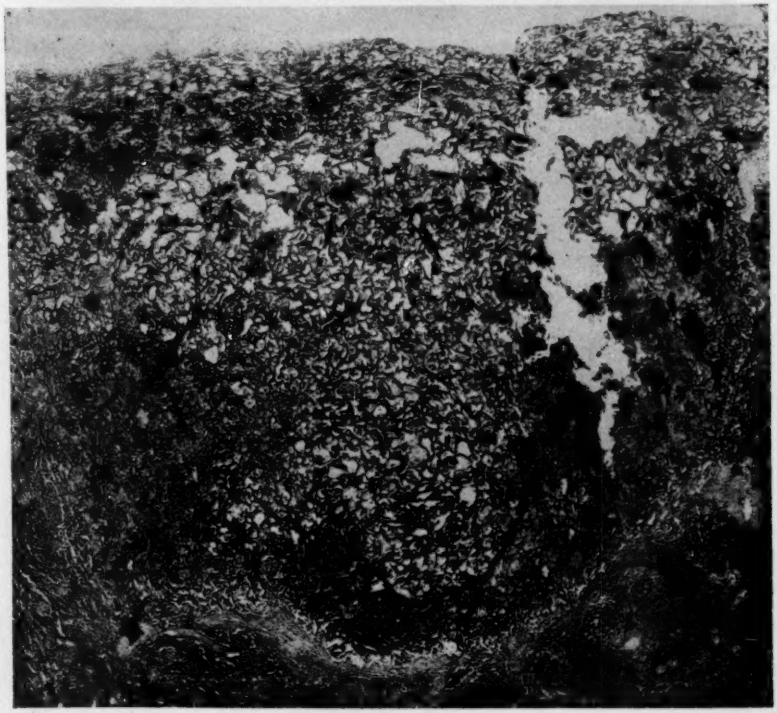

Fig. 6.—Low power photomicrograph showing appearance of gelatin sponge in splenic wound of dog DD2 six days postoperatively. This dog received repository heparin preoperatively and postoperatively and dicumarol® preoperatively, with effect postoperatively. Successful hemostasis of the wound was accomplished by means of a gleatin sponge.

animal the coagulation time at operation was 90 minutes. The animal died on the second postoperative day from external wound hemorrhage. The peritoneal cavity contained no blood. One animal, killed on the seventh postoperative day, had a hematoma of the spleen under the gelatin sponge, but there was no free bleeding (fig. 5).

Repository Heparin and Dicumarol® Preoperatively and Postoperatively (Table 3).—Gelatin sponge effectively controlled the splenic bleeding at the time of operation and postoperatively in four animals whose prothrombin activity ranges and coagulation times were kept close to recognized safe levels (fig. 6). Contrariwise, gelatin sponge failed to control the splenic bleeding at the time of operation in four instances in which the coagulation time ranged from 40 to 120 minutes. In one instance the gelatin sponge appeared effective at the time of operation when the

TABLE 3.—*Efficacy of Gelatin Sponge in Splenic Wounds with Repository Heparin Preoperatively and Postoperatively and Dicumarol® Effect Postoperatively*

Animal No.	Prothrombin Activity at Operation, %	Coagulation Time at Operation, Min.	Postoperative Range Prothrombin Activity, %	Postoperative Range Coagulation Time, Min.	Days Observed	Comment
DD1	100	40	5.8 to 42.4	30 to 40	6	Died of distemper; abdominal cavity normal; abdominal wound hematoma
DD2	100	50	7.8 to 53.6	30 to 50	6	Killed
DD3	100	60 to 80	6.4 to 48	10 to 30	7	Killed; abdominal wound infection
DD4	100	100	.....	.....	..	Died day of operation; marked blood loss and shock
DD5	100	50 to 40	.....	15 to 50	1	Abdomen full of blood; all splenic packs intact; wound hematoma
DD6	100	40 to 60	80	60	1	Died 1st postoperative day; bloody stool; severe blood loss and shock at operation; no blood in abdomen
DD7	100	40 to 20	17.6	20 to 60	1	Died 1st postoperative day; much blood in abdomen; splenic packs intact
DD8	100	40 to 15	9 to 64	15 to 30	6	Prothrombin activity escaped once to 100%; killed
DD10	...	120	.....	.....	1	Splenectomy at operation to control bleeding

coagulation time was 40 minutes, but the animal was found dead from hemorrhage the next morning.

Postmortem examinations on successfully treated animals indicated that in only two, one of which had been treated with dicumarol® alone and one with repository heparin and dicumarol,® was there any evidence of postoperative bleeding in the peritoneal cavity, although this was apparently not severe and the tamponading effect of the gelatin sponge nonetheless proved successful.

Varying degrees of external abdominal wound bleeding were noticed in six animals. In two of the dogs this external bleeding might have contributed to death. In both these dogs the prothrombin activity fell to less than 1% postoperatively and remained at that level until death. Gelatin sponge had not been used in any of the abdominal wounds.

Regarding the control tests in which frayed surgical cotton plaques and coarse mesh gauze were used, we found that cotton had a remarkable hemostatic effect, almost equaling that of gelatin sponge in the various tests. Coarse mesh gauze, on

the other hand, did not control bleeding noticeably. These findings gave us the impression that the fine mesh of interstices in both the gelatin sponge and the cotton is the deciding factor in the efficacy of these substances as hemostatic agents, regardless of whether the fibrinogen phase or the prothrombin phase of coagulation is altered.

TIME FACTOR

In order to establish a time factor for the control of bleeding, pressure was released from the hemostatic substance at regular time intervals and the resumption of bleeding noted. We found that control of bleeding was always noted in less than five minutes, or else the hemostasis was completely ineffectual. This was the case even in some instances when a markedly exaggerated bleeding tendency was induced. When coagulation times or prothrombin levels were exceptionally far beyond recognized therapeutic values, hemostasis could not be effected at any time during the application in periods up to one hour. Hence, if the hemostatic substance was to control bleeding, it always did so in one to five minutes. In heparinized animals this situation held with coagulation times up to 45 minutes and in dogs given dicumarol® with prothrombin levels as low as 2.7 per cent. These levels are considerably beyond the accepted safe ones.

The shortest spontaneous bleeding time for any control wound, free from packing or pressure, in a heparinized dog was 10 minutes. This dog had a coagulation time range of 48 to 32 minutes during operation. Test wounds packed with gelatin sponge in the same animal ceased bleeding within one minute.

The shortest spontaneous bleeding time for any similar control wound in a dog given dicumarol® was 8 minutes 30 seconds. This dog had a prothrombin activity of 13.4 per cent during surgical intervention. Test wounds packed with gelatin sponge in the same animal ceased bleeding within one minute.

SUMMARY AND CONCLUSIONS

Gelatin sponge effectively controlled bleeding from the spleens of dogs in the presence of anticoagulant therapy when coagulation times or prothrombin levels were within or not far beyond recognized safe therapeutic limits. However, when such limits were exceeded to a great extent hemostasis by means of gelatin sponge could not be depended on. Experiences with human beings appear to parallel these findings when gelatin sponge is used to control bleeding in skeletal tissues in the presence of anticoagulant therapy. Our results appear to indicate that when surgery is performed in the presence of anticoagulant therapy gelatin sponge can be depended on for hemostasis of oozing surfaces, provided therapeutic levels of anticoagulant therapy are not exceeded.

DISCUSSION

DR. JOHN OLWIN, Chicago: The work of Drs. Laufman, Preston and Bourdeau should serve further to dispel the fear that some still have of anticoagulants even if they are accurately controlled.

It is necessary, at times, to operate on people who are on anticoagulant therapy or who, for other reasons, have a depressed coagulation function. In fact, in cases of peripheral embolism we give heparin as soon as the diagnosis is made, and we operate on the patient for the removal of the embolus as soon thereafter as possible. Neither do we hesitate to use anticoagulants when indicated in cases of transurethral prostatic resection as short a time as five hours after operation, and as yet we have run into no untoward bleeding. The safety margin in the presence of adequately controlled anticoagulants is, we believe, reasonably wide.

I should like to make two points concerning absorbable sponge materials: First, they act primarily in a postage stamp or tire patch fashion. By their own nature of adhering to surfaces covered with a sticky substance, they seal the tiny capillaries and even larger openings in the vascular system, and thus contain the blood. Heparin acts by interfering with the action of several of the clotting and anticlotting factors. Dicumarol,® according to our present knowledge, acts primarily by depressing prothrombin and, in the early stages, Ac-globulin, which is a powerful accelerator of clotting. Neither drug, however, interferes with a large number of proteins, which, by their very nature, are gluelike. We use egg albumin in the pathology laboratory to cause our sections to adhere to the slide, and I am sure many of you have used the residual albumin in eggs as glue or mucilage. Even in the presence of anticoagulants many of these proteins are unchanged and thus may aid in the tire-patch-like function of absorbable sponges. This situation obtains within the therapeutic limits of the use of anticoagulants. When the therapeutic limits are exceeded, other factors enter the picture; that is, there is a toxic phase, and in this phase increased capillary permeability and capillary fragility are factors. Even without surgery or injury, bleeding may occur in such cases.

The second point is that two of the three commonly available sponge materials, gelfoam® and fibrin foam, are neutral in their reaction. Therefore, they do not inhibit the action of the naturally occurring thrombin, which is the activator of fibrinogen. Thrombin acts optimally at a pH of 7.3, or practically neutral, and is inactivated at a pH of 4.4. Oxidized cellulose, more commonly called oxycel,® is acid in its reaction, and unless it is sufficiently neutralized before being used it will inactivate thrombin. Also, by its acid nature it sets up more tissue reaction than do the other two materials, gelfoam® and fibrin foam. For this as well as for other reasons, gelfoam® is considered the absorbable sponge material of choice in most instances.

URINARY CHLORIDE DETERMINATIONS IN THE ESTIMATION OF THE SALT REQUIREMENTS IN SURGICAL PATIENTS

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AND
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IT HAS been demonstrated in patients with normal kidney function that urinary chloride values usually demonstrate a lack of salt before serum chloride levels fall below normal limits.[1] For this reason, there has been renewed interest in the use of urinary chlorides for computing the salt requirements of the surgical patient. Van Slyke and Evans [1] have reintroduced the Fantus method [2] of determining urinary chloride concentrations as a bedside test and propose that the estimation be made on urine obtained before each infusion. More recently, Evans [3] has suggested that the first morning specimen is a more reliable guide to therapy. This clinic has noted a similar inaccuracy in the implications of the chloride content of random urine specimens when compared with the total daily urinary chloride output. The concentration of single voided specimens was frequently below the desirable level of 3 gm. per liter recommended by Van Slyke and Evans, even though the 24 hour output of sodium chloride was within normal limits. These variations led us to feel that false conclusions might result when salt therapy is being based on the chloride concentration of random voided specimens of urine. It was thought that a further study of the accuracy of the Fantus test and of the physiological variations of urinary chloride concentrations during a 24 hour period might explain these inconsistencies.

As previously emphasized,[1] certain rules of technique must be observed in performing the Fantus test in order to obtain consistent results. The same dropper must be used for measuring the urine and both reagents. The test tubes must be clean, and the dropper must be rinsed thoroughly between solutions to avoid cross contamination. Isotonic sodium chloride solution was used as a control. In order to standardize this technique, small kits were made up for each ward. By this method, easily reproducible endpoints were obtained, and variations of more than 1 gm. of sodium chloride per liter of urine were rarely seen.

From the Surgical Service, University Hospital, Ohio State University College of Medicine.

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Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 1, 1950.

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2. Fantus, J. B.: Fluid Postoperatively: Statistical Study, J. A. M. A. **107**:14 (July 4) 1936.

3. Evans, E. I.: Personal communication to the authors.

The bedside Fantus test was compared with the Volhard-Harvey method (a highly accurate, time-consuming, titration method used for chloride determinations) by simultaneously determining the chloride concentration of one hundred random specimens of urine. Chart 1 compares the two methods; 89 per cent of the specimens tested fell within a zone of 25 per cent variation, the abnormally high and low readings accounting for the remaining 11 per cent. Van Slyke and Evans,[1] as well as Randall, Habif and Lockwood,[4] report a similar range of accuracy for the Fantus test. This margin of error in a simple bedside method indicates that the Fantus test is a sufficiently accurate and reliable method for determining the chloride content of urine.

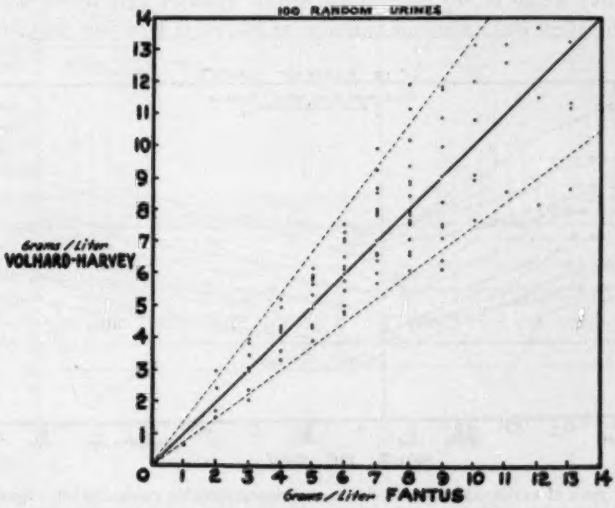

Chart 1.—Comparison of urinary chloride values by Fantus and Volhard-Harvey methods. Note that 89 per cent of these random urine samples tested by both methods fell within the zone of 25 per cent variations, with the higher and the abnormally low readings accounting for the remaining 11 per cent.

Although the bedside Fantus test was used in the studies reported in this paper, more recent experience with the bedside Scribner chloride test [5] indicates that the latter is even more accurate. Therefore we feel that the conclusions reached from the following studies would apply equally well to both bedside methods of urinary chloride determinations.

4. Randall, H. T.; Habif, D. V., and Lockwood, J. S.: Sodium Deficiency in Surgical Patients and the Failure of Urine Chloride as a Guide to Parenteral Therapy, Surgery **28**: 182, 1950.

5. Scribner, B. H.: Bedside Determination of Chloride: A Method for Plasma, Urine and Other Fluids and Its Application to Fluid Balance Problems, Proc. Staff Meet., Mayo Clin. **25**:209, 1950.

VARIATIONS IN URINARY CHLORIDE CONCENTRATION IN NORMAL PATIENTS DURING A TWENTY-FOUR HOUR PERIOD

It has been observed that urinary chloride concentrations are frequently greatest in the early morning. A definite correlation between daily fluctuation of urinary chlorides and urinary volume has been noted, indicating a relationship between the urinary chloride concentration and the fluid intake. In order to investigate this relationship and its effect on the clinical usefulness of the Fantus test, the effect of oral and intravenous fluid intake on urinary chloride values in normal patients was studied.

The Effect of Oral Intake of Fluids.—The investigation of the effect of oral fluid intake was undertaken over a three day period in each of six patients (ages 24 to 57 years) whose kidney function and serum chlorides were within normal limits. Each patient had undergone operation or trauma at least four days previ-

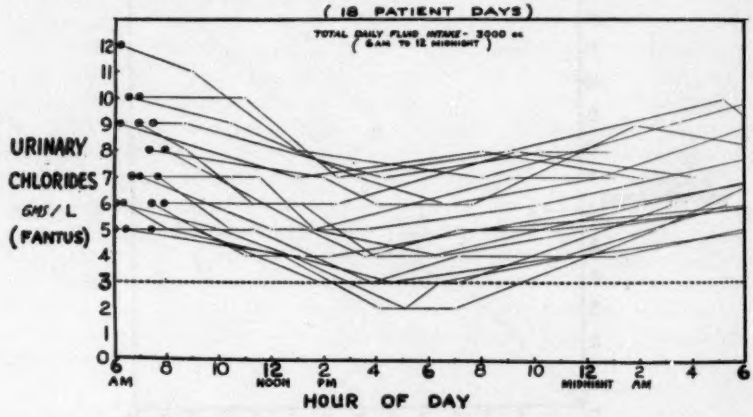

Chart 2.—Effect of orally administered fluids on urinary chloride concentration. Even in normal patients receiving fluids by mouth urinary chlorides may fall below the critical level of 3 gm. per liter. Note the consistent levels above the critical level (encircled dots) of first voided specimens of urine in the morning.

ously and was on a regular hospital diet containing 6 to 8 gm. of salt daily. Each patient received a total of 3,000 cc. of fluid orally (including that in meals) distributed between 6 a. m. and 12 midnight according to his wants. The chloride concentration of each voided specimen of urine was determined by the Fantus test. Representing each day of the study as one patient day, chart 2 is a composite of the chloride concentrations of each voided urine specimen for the 18 patient days.

Every patient on each of the three days showed a definite lowering of urinary chloride concentration (in some instances below the 3 gm. per liter level) after he began to drink fluids. The periods of lowest urinary chloride concentration coincided with the periods of greatest urinary volume. This indicated that the reduced chloride concentration resulted from the dilution effect of the water-induecd diuresis. The reciprocal relationship between the urinary chloride concentration and the urinary volume was a constant finding in our studies and in those of others.[4]

Therefore, as might be expected, the first voided specimen in the morning, unaffected by fluid intake, contained the most chloride. This decrement in urinary chloriue concentration following the administration of fluid to a patient in normal electrolyte balance is significant because the value, being below the 3 gm. per liter level, falsely denotes a need for salt therapy. On the other hand, the first voided specimen after 6 a. m. (represented by encircled dots in chart 2) consistently contained a chloride content well above 3 gm. per liter, correctly indicating that no salt deficit existed. It would appear that the method of application of the Fantus test, as suggested by Van Slyke and Evans,[1] is valid only for the first morning urine specimen before food and fluid have been taken.

The Effect of Intravenous Intake of Fluids.—The effect of the commonly used fluids given intravenously on urinary chloride excretion was observed in patients

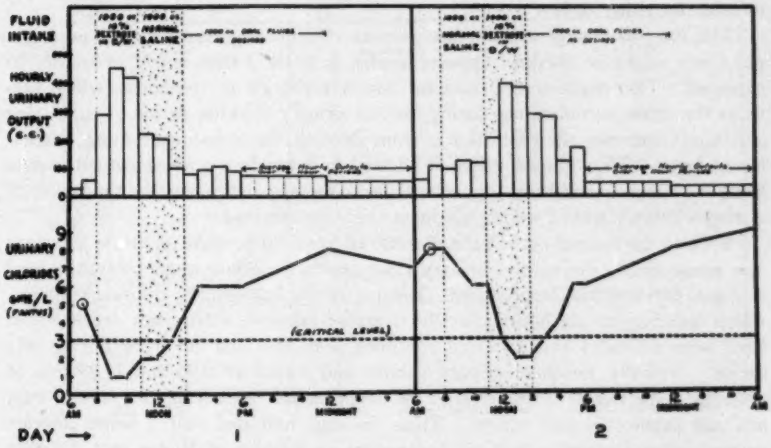

Chart 3.—Effect of intravenous administration of fluids on urinary chloride concentrations. Diuresis resulting from the administration of 10 per cent dextrose in distilled water caused a consistent lowering of urinary chloride concentration below the critical level. This effect was not seen with isotonic sodium chloride solution. First voided specimens in the morning (encircled dots) denoted correctly that no salt existed.

with normal renal function and in whom there was no demonstrable fluid or electrolyte problem. All these patients were well hydrated, had normal serum chloride levels and had undergone operation or trauma at least four days previously. Chart 3 illustrates the results in a 34 year old white man who had sustained a compression fracture of the twelfth dorsal vertebra and in whom it was possible to collect hourly urine specimens by means of an indwelling catheter inserted for the relief of temporary urinary retention. During each of the two experimental days, 2,000 cc. of fluid (1 liter of 10 per cent dextrose in distilled water and 1 liter of isotonic sodium chloride solution) were given intravenously, in addition to 1,000 cc. of fluid orally (including meals). Coffee, tea and carbonated drinks were withheld during the study to prevent their diuretic effect. Urine samples were collected hourly from 6 a. m. to 6 p. m. and at six hour intervals for the remaining 12

hours. The chloride concentration of each specimen was determined by the Fantus test. The rate of dextrose infusion was never greater than 0.5 gm. per kilogram of body weight per hour. Glycosuria did not occur, a fact which is consistent with the findings of Lockhart and Elman.[6]

On the first day, a liter of 10 per cent dextrose in distilled water was infused over a three hour period followed by a liter of isotonic sodium chloride solution at the same rate. To evaluate the effect of changing the order of administration of the solutions on urinary chloride and volume output, the sequence of administration was reversed on the second day. On both days diuresis accompanied and followed the period of dextrose infusion and was of the same duration and volume regardless of the order of administration of the two solutions. The dextrose infusion on each day produced such marked diuresis that the urinary chloride fell below 3 gm. per liter for several hours. No such diuretic effect was noted during the saline infusion on either day.

The interval during which a low urinary chloride concentration (below 3 gm. per liter) might be obtained appears briefer in chart 3 than would ordinarily be expected. This result comes from the hourly collection of specimens, which prevents the urine, accumulating during the low urinary chloride period (i. e., during and after dextrose administration), from diluting the subsequent more concentrated urine. This dilution effect, if allowed to occur in a voiding patient, would bring more specimens below the critical level, thereby increasing the time interval during which an invalid voided specimen might be obtained.

Even in the normal patient the diuretic effect of 10 per cent dextrose infusions may cause such a decrease of urinary chlorides that concentrations below the level of 3 gm. per liter will be produced. Because of the low urinary chloride readings, which lasted up to six hours after the dextrose infusion, a false salt deficit would have been indicated had a voided specimen been obtained any time during this period. Actually, adequate urinary volume and a total of 9.96 and 11.89 gm. of chloride, respectively, during each of the experimental days denoted a normal fluid and salt balance in this patient. These findings indicated that a urine chloride determination obtained within six hours after an infusion of 10 per cent dextrose in distilled water will not accurately reflect the state of salt balance in normal patients. This fact is true even when the infusion is given slowly so as not to produce glycosuria. On the other hand, the early morning urine samples correctly indicated that the patient was not suffering from salt deficiency.

The effect of single dextrose infusions on the urinary chloride concentrations of normal subjects was observed in five additional patients whose ages ranged from 19 to 64. Each patient was given a liter of 10 per cent dextrose in distilled water on the first experimental day, 5 per cent dextrose in distilled water on the second day and 5 per cent dextrose in isotonic sodium chloride solution on the third day. Nothing by mouth was permitted from midnight until after the infusions were completed. Each infusion ran from 8 a. m. to 11 a. m., after which the patients were given a regular diet and a total of 2,000 cc. of fluids orally during the remainder of the 24 hour period. The time of each voided specimen was recorded and its chloride concentration determined by the Fantus method. Chart 4 illustrates the results. On the first day, in three of five patients, the chloride concentration

6. Lockhart, C. E., and Elman, R.: The Effect of Intravenous Glucose and Amino Acids on Glycosuria and Urinary Output in Humans, Surg., Gynec. & Obst. **88**:97, 1949.

of the first specimen of urine voided after the completion of the infusion of 10 per cent dextrose in distilled water fell below the desired level and some remained below this level for as long as 12 hours. On the second day, two of five of the first specimens following the infusion of 5 per cent dextrose in distilled water had concentrations which dropped below 3 gm. per liter and remained there for as long as six hours. If the clinician were planning to follow either of these infusions with more intravenously administered fluids, urinary chloride levels prior to each infusion would have prompted him to administer saline. This saline would have been unnecessary as demonstrated by the adequate daily outputs of salt, which ranged from 8.2 to 11.7 gm. per patient. However, when 5 per cent dextrose in isotonic sodium chloride was given on the third day, no consistent lowering of urinary chloride concentration was noted. This result may be due to the hydrating action

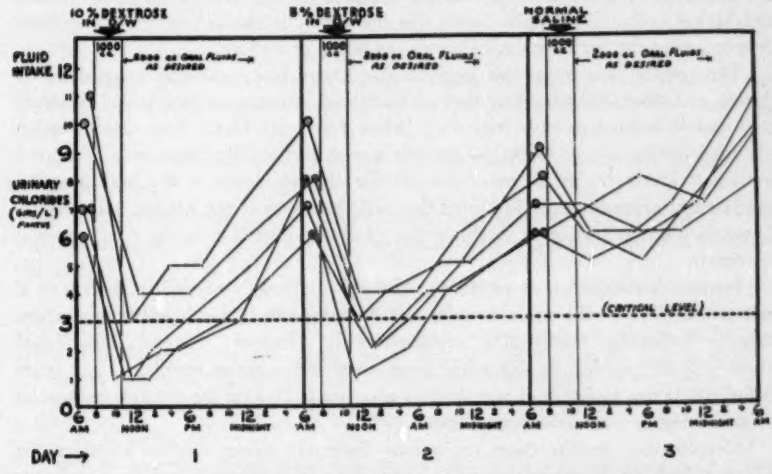

Chart 4.—Effect of intravenously administered fluids on urinary chloride concentration; comparison of commonly used solutions given intravenously. Approximately 50 per cent of the first voided urine specimens after infusions of 5 or 10 per cent dextrose in distilled water showed a false need for salt, with chloride levels falling below 3 gm. per liter. Testing of the first voided morning specimens (encircled dots) would have consistently prevented this discrepancy.

of saline offsetting the diuretic action of dextrose,[7] or perhaps to the excretion of infused chlorides. The evidence from this series of patients suggests that if the Fantus test is to be used to estimate the salt needs of a patient it should not be used for urine specimens obtained the same day after dextrose solutions in distilled water had been given.

COMMENT

The clinician is constantly faced with the threat of salt deficiency during the management of electrolyte problems in surgical patients.[8] This problem is com-

7. Stewart, J. D., and Rourke, G. M.: The Effects of Large Intravenous Infusions on Body Fluids, J. Clin. Invest. **21**:197, 1942.

8. Peters, J. P.: The Treatment of Salt Depletion, Surgery **24**:568, 1948. Ireneus, C., Jr.: The Hypochloremic State in Surgical Patients, Surgery **18**:582, 1945.

plicated by the effects which might result from administering too much salt.[9] Van Slyke and Evans,[1] in their studies of salt depletion in human volunteers, demonstrated that urinary chloride determinations will reflect a salt deficit before the serum chlorides become reduced. These authors recommended the employment of urinary chloride values of single samples as an index to salt therapy. Such a test would have many practical advantages. It obviates the uncertainties of a 24 hour collection of urine; it helps to reduce the delay in therapy because of its rapid bedside technique, and the patient is spared the discomfort of repeated venipunctures and much of the expense of repeated laboratory procedures.

However, all clinicians agree that the correct interpretation of urinary chloride values depends on unimpaired renal function and the absence of conditions in which there is even temporary renal impairment. Extreme dehydration, shock and the immediate postoperative period are included among these conditions. Coller and Moyer and others [10] have shown that the kidney is unable to excrete an excess of salt during the first few days after an operative procedure.

The results of our studies suggest that the urinary chloride concentrations during and after oral administration of fluids and intravenous infusion of dextrose solutions in normal patients may drop below 3 gm. per liter. Any determination obtained during one of these low periods would give a false impression of a need for salt. However, in all cases studied the chloride level of the first morning specimen of urine correctly indicated that salt therapy was not needed. Therefore, it would seem advisable to limit the use of the Fantus test to the first morning specimen.

Further investigation of patients exhibiting salt lack is needed to determine if salt will appear in the urine in sufficient quantities during saline administration, thereby indicating falsely that replacement is adequate. Several unpublished studies of the problem in this clinic have given inconclusive results. Until more definite data are available, it would seem wise not to rely on the chloride content of urine during or soon after any infusion.

Nevertheless, despite these limitations there are many surgical situations in which a bedside determination of urinary chloride content should be a valuable aid to therapy. This is particularly true of some of the lengthy problems in electrolyte balance resulting from prolonged vomiting, diarrhea, drainage from the gastrointestinal or biliary tracts and burned surfaces. Because of the sensitivity of the normal kidney even to a mild salt deficit, this test should make it possible to detect salt deficiency before symptoms of reduced serum chloride levels appear.

If the limitations of the Fantus test are borne in mind, it may be used successfully as follows: In patients presenting problems of salt replacement, the first morning-voided specimen is tested for its chloride concentration. If the urine contains less than 3 gm. per liter, a salt deficiency is assumed. A blood sample for serum chloride determination is drawn in order to ascertain more accurately

9. Coller, F. A.; Iob, L. V.; Vaughn, H. H.; Kalder, N. B., and Moyer, C. A.: Translocation of Fluid Produced by the Intravenous Administration of Isotonic Salt Solutions in Man Postoperatively, Ann. Surg. **122**:663, 1945.

10. Moyer, C. A.; Coller, F. A.; Iob, V.; Bryant, L.; Vaughn, H.; Kalder, N. B., and Berry, R. E. L.: Some Effects of Operation, Anesthesia and Composition of Parenteral Fluids upon the Excretion of Water and Salt, South. Surgeon **15**:218, 1949. Coller and others.[9]

the magnitude of salt deficit.[1] Salt replacement may then be started and the total amount to be given decided after the serum chloride value is reported by the laboratory. If the serum chloride is also found to be low, vigorous salt replacement is indicated. If the serum level is unaltered, smaller amounts of saline will suffice. If it becomes necessary to estimate the chloride status of a patient after he has received fluids either orally or intravenously during that day, a serum chloride determination is the more reliable index to therapy.

In cases in which sodium and potassium imbalances are serious, the urinary chloride studies themselves will not give sufficient information.[4] The determinations of these cations are difficult and require spectrophotometric methods to assure accuracy. However, in many of the smaller hospitals the surgeon may have to rely heavily on such simplified methods as the Fantus test. Even in large medical centers, there is a definite need for simplified methods of handling the routine salt problem.

CONCLUSIONS

1. Diuresis following orally administered fluids or intravenously administered dextrose solutions invalidates the use of urinary chloride concentration as an index to salt need.

2. These factors may be avoided by limiting such determinations to the first voided morning urinary specimens.

3. If the morning urinary chloride concentration is below 3 gm. per liter, blood should be drawn for a serum chloride determination and the first infusion, containing salt, should be started.

DISCUSSION

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: As Dr. Reimers said, we feel that the determination of the chloride in the urine on the first morning specimen can give the clinician valuable information. I believe that past criticism of the test has stemmed from the fact that we have expected too much from such a simple procedure. Although the Fantus test is reasonably accurate, the test as described by Dr. Scribner is much more reliable and is the method we intend to use in the future.

One main advantage, I feel, arises from the fact that young surgeons or interns who are expected to determine urinary chlorides on the first morning-voided specimen become more alert to the electrolyte problem. In turn, the necessary intravenous infusions of fluids can be ordered before he goes to the operating room.

Secondly, as Dr. Reimers has pointed out, those chronically ill patients requiring many venipunctures certainly appreciate any type of test which would decrease the punishment which they must go through. Any simplified test such as this, which can be made to fit the needs of the patient and make him more comfortable on occasion, is worthy of clinical application.

On the other hand, the surgeon accepting the responsibility of carrying out major abdominal operations should have access to all types of modern laboratory facilities, including a flame photometer.

BLOOD CONSERVATION BY AUTOTRANSFUSION

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OMAHA

THIS report deals with an experience in 28 cases in which an improved technic of autotransfusion was used. A simple method is used to collect blood from an operative site and return it immediately to the patient by the intravenous route. This is not an original endeavor. Johannes Theis,[1] of Leipzig, Germany, is credited with the first use of autotransfusion for ruptured ectopic gestation in 1914. For a clean pool of blood he used the open, dipping, straining and citrating method. It involved the surgeon in an inefficient, time-consuming, awkward and surgically distracting job. The procedure was adopted in Europe, particularly in Germany. The complicated endeavor was rarely employed in this country; the largest series consisted of 21 cases reported in 1925[2] by Davis and Cushing. A simple safe method would probably find considerable favor.

A review of the literature on the 467 autotransfusions to date[3] is worthy of two comments. First, there is consistent evidence that a small quantity of blood returned to the patient has remarkable recuperative and resuscitative powers. No reason was attributed for the unusual refreshment. Secondly, autotransfusion has been a safe procedure; significant transfusion reactions were not noted.

In this series a closed vacuum method was improvised by incorporating a sterile donor transfusion set into a suction system. The needed apparatus (Figs. 1 and 2) is on hand in every hospital in the country. It consists of a Yankauer tonsil suction unit, two gallbladder trocars (Ochsner, size 16 F.) and a No. 13 gage needle.

TECHNIQUE

The apparatus is assembled under sterile technique. A surgical assistant operates the suction in the operative site, where the use of sponges and hemostats is restricted. The suction machine, collecting vessel and citrate drip bottle are operated from the head of the table by the anesthesia team.

The elimination of the old open method reduces the chances of contamination. The vacuum system has advantages and disadvantages over the dipping method. It

From the University of Nebraska College of Medicine.

This article is based on work done at St. Joseph's Hospital and Creighton School of Medicine.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 2, 1950.

1. Thies, J.: Zentralbl. Gynäk. **38**:1191, 1914.

2. Davis, L. E., and Cushing, H.: Surg., Gynec. & Obst. **40**:310, 1925.

3. (*a*) Ricci, J. V., and Di Palma, S.: Am. J. Obst. & Gynec. **22**:857, 1931. (*b*) LeFebure, F.: Internat. Abstr. Surg. **84**:583, 1947; Presse méd. **54**:833, 1946. (*c*) Negovsky, V. A.: Am. Rev. Soviet Med. **2**:303, 1945.

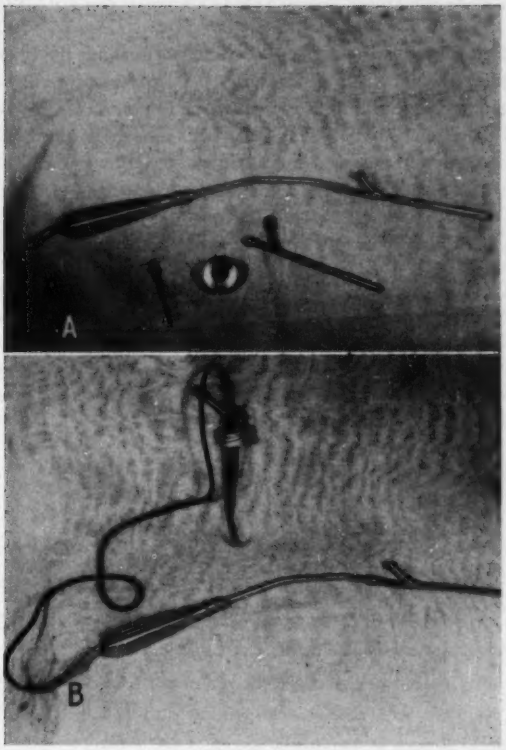

Fig. 1.—Autotransfusion apparatus. *A*, assembly used to house the plastic tubing for collecting surgical blood. *B*, plastic tubing in place for aspirating blood.

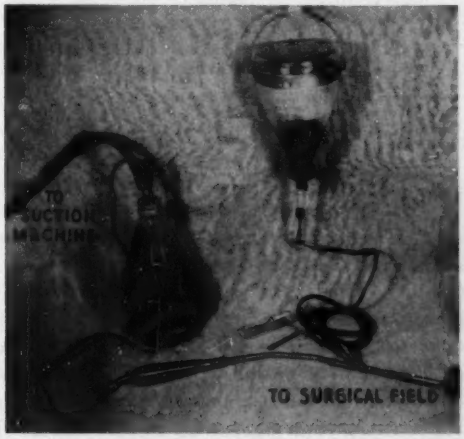

Fig. 2.—The standing bottle collects blood (when ready for venoclysis, it is disconnected from this system and adapted with a filter and tubing as in ordinary transfusion). The hanging bottle holds citrate solution that drips to the site of the bleeding.

can collect and transport blood efficiently without disturbing the operation, leaving the surgical team free for their usual duties. However, aspiration does produce bothersome foaming and frothing in the collecting bottle. This has been controlled by preliminary placing of small floating glass balls into the flask, thereby promoting a mechanical separation of the foam and fibrin mass that tends to float. The heavier liquid blood then settles to the bottom and tends to be free of clotting without anticoagulants. Another important factor is that vacuum produces more hemolysis than dipping. It is in direct proportion to the amount of suction used. Ordinarily 4 to

Summary of Twenty-Eight Surgical Cases with Revascularization of Blood

Patient	Age	Operation	Amount of Blood Revascularized, Cc.	Donor Blood Transfusion	Clinical Reaction
R. D.	32	Cholecystectomy; appendectomy	600	0	None
P. G.	57	Cholecystectomy; appendectomy	200	0	None
N. W.	52	Cholecystectomy; appendectomy	250	0	None
E. B.	52	Myomectomy; appendectomy	150	0	None
M. F.	18	Cesarean section	400	0	None
G. K.	26	Removal of protruding intervertebral disk	350	0	None
G. S.	32	Removal of protruding intervertebral disk	300	0	None
J. R.	40	Removal of protruding intervertebral disk	350	0	None
J. M.	40	Removal of protruding intervertebral disk	600	0	None
C. Y.	55	Retropubic prostatectomy	750	0	None
W. S.	33	Removal of protruding intervertebral disk	900	0	None
J. H.	68	Retropubic prostatectomy	250	0	None
S. L.	29	Removal of protruding intervertebral disk and fusion	600	0	None
V. C.	67	Abdominal hernia	150	0	None
M. C.	44	Nephrectomy	150	0	None
M. L.	29	Removal of protruding intervertebral disk and fusion	725	0	None
B. J.	46	Removal of protruding intervertebral disk and fusion	1,000	0	None
L. K.	40	Removal of intervertebral disk	1,200	0	None
G. V.	23	Cesarean section	400	0	None
M. P.	32	Removal of protruding intervertebral disk and fusion	1,200	0	None
J. C.	41	Removal of protruding intervertebral disk	900	0	None
L. H.	54	Gastric resection	150	0	None
G. S.	30	Removal of protruding intervertebral disk	300	0	None
J. R.	28	Removal of protruding intervertebral disk	350	0	None
S. L.	29	Removal of protruding intervertebral disk and fusion	1,475	250 cc.	Severe hematuria
A. M.	38	Removal of protruding intervertebral disk and fusion	650	500 cc.	Severe hematuria
N. D.	87	Nailing fractured hip	150	1,000 cc.	None
A. C.	12	Removal of tumor, mediastinal	1,000	1,500 cc.	None

6 lb. (1.8 to 2.7 kg.) of negative pressure will break down about 0.4 to 0.6 gm. of hemoglobin per 100 cc. These lower limits of hemolysis were tolerated in this small series.

SUMMARY OF TWENTY-EIGHT CASES OF REVASCULARIZATION

In the 28 cases a total of 13,000 cc., or 26 pints, of surgical blood was revascularized. The quantities varied from 150 to 1,475 cc. per patient. The ages of the patients varied from 12 to 87 years. The procedure was used in all types of clean surgical procedures. Fifteen operations were for protrusion of intervertebral disks. In 24 procedures the patient's own blood was transfused, with no reactions. The group appeared refreshed out of proportion to the volume restored. Subnormal

blood pressures were readily raised, the most remarkable case being one in which the pressure was elevated from 60 mm. systolic to 120 mm. by 200 cc. of blood. The reason for this elevation is not clear. Clinically, it is consistent with work that has been done in treating shock with intravenous administration of oxygenated donor blood,[4] a most difficult problem. That autotransfused blood is highly oxygenated was suspected and subsequently shown by oxygen determinations on simultaneously collected specimens; one sample of blood was taken from the saphenous vein while another was being collected from the site of an abdominal hysterectomy. The venous sample had 16 vol. % of oxygen while the surgical field blood had 23 vol. %. This highly oxygenated character of autotransfused blood has not been previously described. It may be the reason for its remarkable recuperative powers.

In the four patients receiving donor blood in addition to their own, two reactions occurred. One patient had 1,475 cc. of her own blood returned during an operation, the largest quantity in this series. Administration of donor blood was started, and half a pint (250 cc.) was given when she began to chill. Hematuria, and a markedly reduced urinary output developed, and the nonprotein nitrogen level was increased to 49.5 mg. per 100 cc. In two weeks, normal kidney function returned and the patient recovered. The second patient suffered from similar hematuria and kidney shutdown with recovery. Donor blood (500 cc.) was given with the anesthesia because of some anemia. A recheck of typing and crossmatching failed to show incompatibility. Laboratory tests showed hemolysis to be present in both types of blood given. It seems reasonable to assume that the reactions were due to extravascular hemolysis present in both types of blood given. Inadvertently, 10 to 12 lb. (4.5 to 5.4 kg.) of negative pressure was used for vacuum collecting in these two cases, returning blood that was unnecessarily hemolyzed to the extent of 1.0 and 1.4 gm. per 100 cc., respectively.

COMMENT

This is a report of the development and use of a simplified closed method for autotransfusion in a small series of cases. It is not intended to suggest the use of this system for every surgical case but rather to stimulate interest and investigation into the problems of salvaging wasted human blood which may be considered ideally compatible with the patient without the need of laboratory work or donor blood. No delay of time for procuring, typing, crossmatching or for serologic study is needed.

The vacuum system affords a convenience in collecting blood, but it does produce some hemolysis that deserves restraint in the amount of suction used. In addition to restoring freshly lost circulatory volume, this method offers a study of a problem inherent in the use of donor blood i. e., the use of oxygenated blood intravenously in shock. To date, oxygenating stored blood has been impractical.[4a] Attention has not been called to the already oxygenated character of the blood from the surgical field. Autotransfusion in small quantities of a pint or less seems safe and exceptionally therapeutic.

4. Jacobi, M., and others: Effect of Intravenous Administration of Oxygen on Shock in Dogs and Human Beings, Arch. Surg. **52**:42 (Jan.) 1946. Ziegler, E. E.: J. Lab. & Clin. Med. **27**:223, 1941. Tunnicliffe, F. W., and Stebbing, G. F.: Lancet **2**:321, 1916. Clark, L. C., Jr.; Gollan, F., and Gupta, V. B.: Science **3**:85 (Jan. 27) 1950.

SUMMARY AND CONCLUSIONS

A simpler, closed system of autotransfusion in 28 cases has been described. It can be assembled with the ordinary equipment at hand in any hospital.

The hemolysis and the oxygenated character of free surgical blood for such transvascularization make investigation of its pathological and therapeutic potentials worth while.

Autotransfusion could be an additional aid when active exsanguination is encountered in clean surgical cases, particularly when there is no hope of other aid.

DISCUSSION

Dr. Eugene A. Osius, Detroit: This paper shows ingenuity and in my opinion has practical value.

Dr. J. Dewey Bisgard, Omaha: I watched Dr. Stager in the process of developing this technic during the past year and asked him if he would present it here. He was a little reluctant because he wanted to carry on more studies and investigate it further. I can conceive of a situation (a very probable one with a war in progress) in which there would be such a demand for blood that the usual channels could not meet the demand, and it might be desirable to conserve blood which every day we are throwing away and wasting.

CYSTIC HYGROMAS OF THE NECK

KENNETH C. SAWYER, M.D.
AND
ROBERT WOODRUFF, M.D.
DENVER

CYSTIC hygromas of the neck continue to present a problem and a challenge to surgeons, especially from the standpoint of management. Hygromas are benign, multilocular, cystic tumors of lymphatic origin with a lining of endothelium, and although they have been recognized as a pathological entity for many years, the medical literature on this subject has been limited. It is our purpose to review briefly the background of cystic hygromas and to offer suggestions in management based on experiences with eight cases in the past four years.

There have been many theories and explanations for these growths. In 1843 Wernher [1] described them as new growths and gave a good description of their clinical course. However, it was not until the monumental work of Sabin [2] on the development of the lymphatic system that the real basis for cystic hygroma formation was established. According to Sabin's theory, a capillary plexus is formed from each jugular vein during the primary stage of development. Portions of these plexuses break off, and from these segments the jugular sacs develop on each side. This development is the beginning of the lymphatic system. McClure and Silvester [3] and Goetsch (cited by Callister)[4] have shown that through some anomaly of growth, accident or fibrosis portions of the jugular sacs fail to establish a communication with the venous system. Hence, free areas of lymphatic tissue which retain the inherent property of growth and penetration exist in the cervical region. Goetsch also demonstrated that hygroma cysts arise primarily from membranous sprouts derived from the walls of cystic spaces which are already present. These sprouts penetrate and permeate into surrounding tissues and eventually become canalized and form additional cysts. Pressure which causes necrosis of surrounding tissues is

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 2, 1950.

1. Wernher, A.: Die angeborenen Kysten-Hygrome und die ihnen verwandten Geschwülste in anatomischer diagnostischer und therapeutischer Beziehung, Giessen, G. F. Heyer, Vater, 1843; cited by Ward, G. E.; Hendricks, J. W., and Chambers, R. G.: West. J. Surg. **58**:41-47 (Feb.) 1950.

2. Sabin, F.: Development of the Lymphatic System, in Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, pp. 709-716.

3. McClure, C. F. W., and Silvester, C. F.: A Comparative Study of the Lymphatico-Venous Communication in Adult Mammals, Anat. Rec. **3**:534-552, 1909.

4. Callister, A. C.: Hygroma Colli Cysticum, Rocky Mountain M. J. **38**:562-564 (July) 1941.

produced by these small cysts. They may even engulf the remnants of necrotic areas. Thus, it can be readily understood why a growing cyst can enlarge rapidly and infiltrate extensively in a short time, even in babies and young children.

This presentation is based on our experience in management of eight patients with hygromas of the neck, the first of whom was seen in 1946. The follow-up of these cases is necessarily of rather short duration. The tumors have been found oftener in females than in males and in children more frequently than in adults. In this series there were five females and three males. Four, or 50 per cent, of the tumors were in children. The neck is the commonest site for hygroma formation, but they occasionally develop in the retroperitoneal tissue, groin, popliteal space or axilla.

Usually patients give a history of a painless tumor in some region of the neck. The growth may have been slow or rapid, and sometimes the history indicates that hygromas have disappeared for weeks or months, only to reappear without apparent

Fig. 1.—Preoperative photograph of tumor in the neck of a 6 week old girl.

cause. The involvement of sensory nerves occasionally alters the picture. Often the tumor is noticed first soon after birth. Our youngest patient was a 6 weeks old baby, and the oldest patient was 38 years of age. The duration of the symptoms was from two weeks to 20 years.

On examination, one detects a soft, multilocular cystic tumor. It often is adherent to the skin and may penetrate deep into the neck and extend into the mediastinum. Extensions to the axilla are not uncommon.

The walls of the new cysts are thin, fragile and transparent. Older cysts become thick and fibrotic and as a result of their permeating growth often contain muscle, nerve and other tissues. The content is usually a serous, watery, straw-colored fluid. The cysts are lined with endothelium, and they sometimes become infected, with resulting cellular infiltration into their walls. The diagnosis is not difficult. However, hygromas must be differentiated from branchial cleft cysts, thyroglossal duct cysts, lymphomas and secondary metastatic cervical neoplasms.

Several methods of treatment have been tried in the management of these lesions. Aspiration as well as incision and drainage have had their advocates. Neither gives permanent relief, and secondary infection has been a serious and even fatal complication. Expectant treatment occasionally meets success inasmuch as some tumors fail to grow and even recede. However, the probability of rapid growth with its sequela or reappearance after recession makes a conservative course unwise.

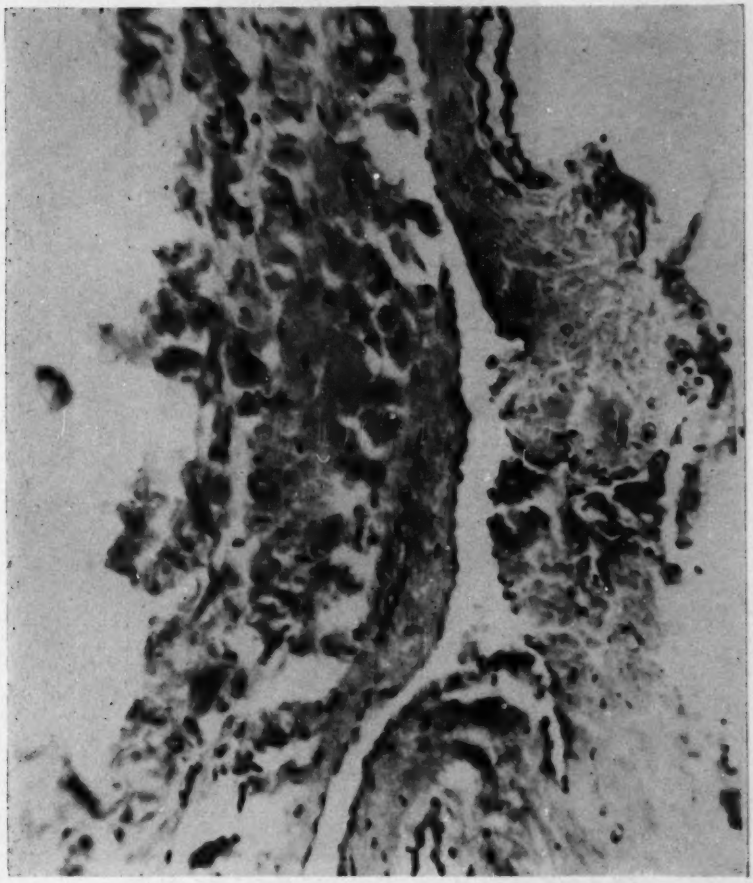

Fig. 2.—Photomicrograph of tumor in figure 1.

In 1929 Figi [5] reported on 13 patients treated with radium at the Mayo Clinic and concluded that this treatment was the most satisfactory type. Seven of the series died subsequently with secondary infection. Inasmuch as mature tissue of

5. Figi, F. A.: Radium in the Treatment of Multilocular Lymph Cysts of Neck in Children, Am. J. Roentgenol. **21**:473-480 (May) 1929.

this nature is inherently radioresistant, it is difficult to expect any effect but some fibrosis from the use of irradiation. Callister is of the opinion, after his experience with a particularly extensive infiltrating lesion, that surgical excision may sometimes be impossible. Ward, Hendrick and Chambers [6] report excellent results from surgical

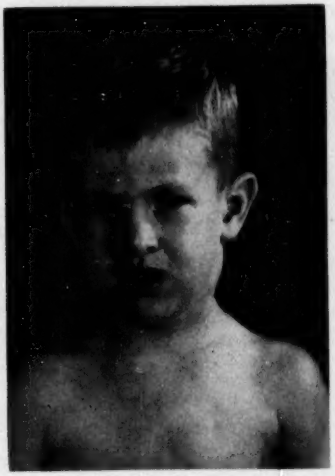

Fig. 3.—Tumor in the neck of 3 year old boy.

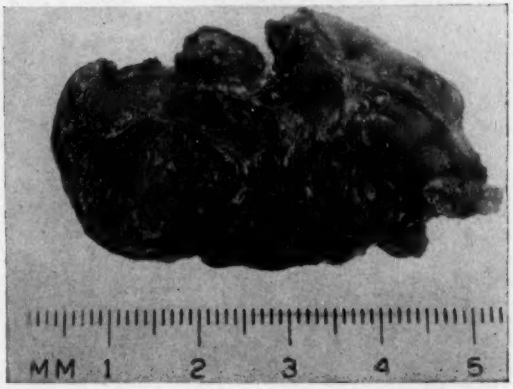

Fig. 4.—Photograph of specimen removed from 3 year old boy.

excision in all their 20 cases. Injections with sclerosing solution followed by surgical removal in three to six weeks has been advocated by some.

6. Ward, G. E.; Hendrick, J. W., and Chambers, R. G.: Cystic Hygroma of the Neck, West. J. Surg. **58**:41-47 (Feb.) 1950.

The hygromas in all cases in this series were excised surgically. Excision of tumor tissue must be complete, and all ramifications must be followed and be completely removed if recurrence is to be avoided. In the past, too little emphasis has been placed on the importance of early removal, and we particularly wish to stress this point. Patients operated on shortly after discovery of the tumor were found to have thin-walled growths, confined to contiguous fascial spaces; these growths were removed without difficulty. On the other hand, in cases in which there had been

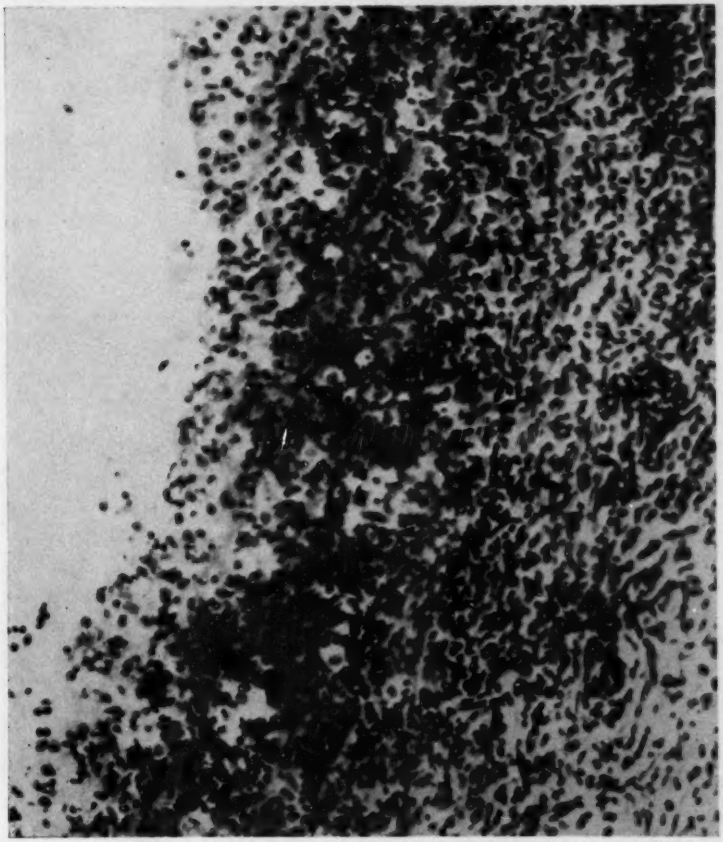

Fig. 5.—Microscopic section of tumor in figure 3.

delay, the lesion had progressed and invaded the surrounding tissues. At operation, instead of a well localized thin-walled cyst, a thick-walled invasive lesion which had permeated extensively, engulfing nerves, blood vessels and other vital structures, was encountered. A surgical procedure which should have been simple had thus been converted into a long, hazardous, major operation with much less chance of success. Five cases in our series illustrate this point.

Fig. 6.—Tumor in the neck of 10 month old boy.

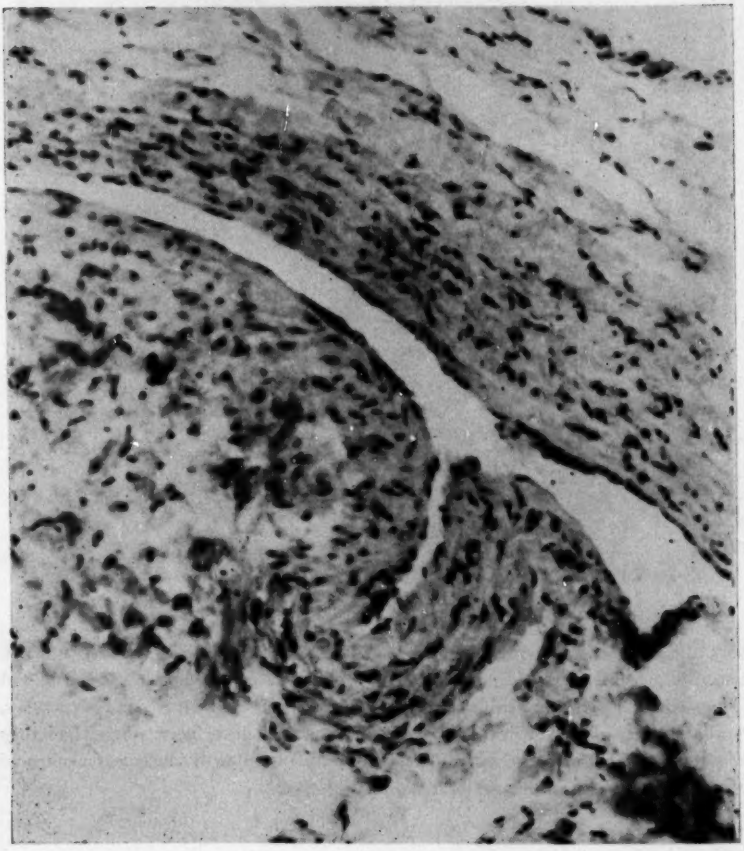

Fig. 7.—Photomicrograph of tumor in figure 6.

A 6 week old girl was seen two weeks after the parents noticed a mass in her neck which had gradually increased in size. Figure 1 is a preoperative photograph. Examination revealed a 3.5 cm. tumor in the suprasternal region. At operation two days later, a thin-walled cystic hygroma was easily excised notwithstanding the fact that it extended into the anterior mediastinum and deep to the carotid vessels.

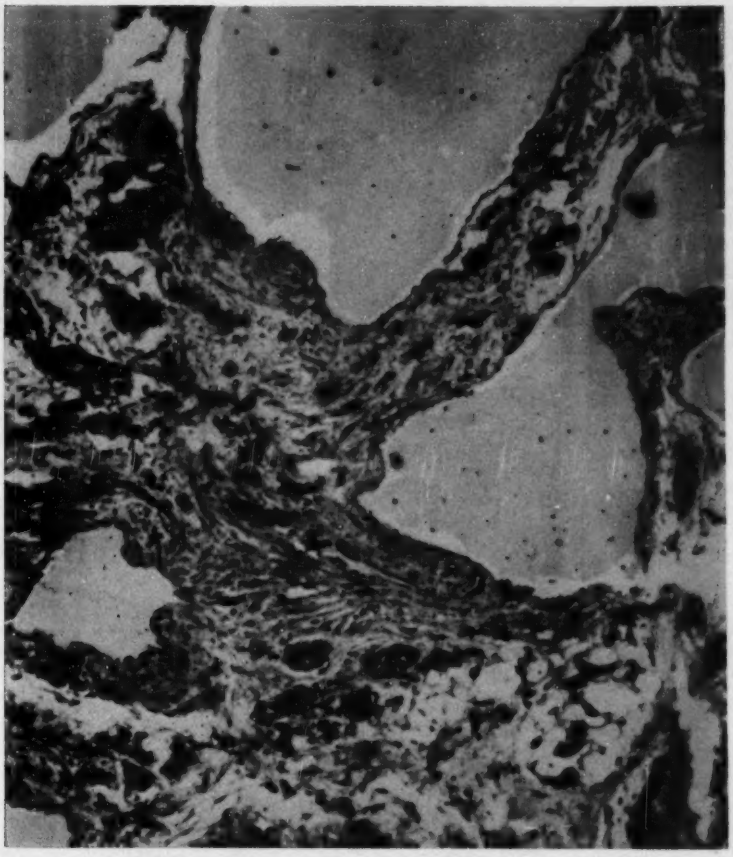

Fig. 8.—Section from lesion in 33 year old man.

There was little infiltration into the neighboring tissues. Microscopic examination (fig. 2) showed a loosely arranged, thin, fibrous connective tissue wall with a lining of endothelial cells.

Contrast this case with that of a 3 year old boy whose parents had noted a growing tumor in the neck for a period of two years (fig. 3). On examination, a subcutaneous cystic mass on the left side of the neck which protruded anterior to

the sternomastoid muscle was demonstrated. At operation, an extensive fibrocystic tumor with many projections which extended into the superior mediastinum and as far upward as the region of the foramen magnum was encountered. The mass was firmly fixed to the surrounding tissues. Blood vessels were engulfed, and excision of a portion of the internal jugular vein was necessary, which resulted in a long and tedious dissection. Figure 4 is a photograph of the specimen. There

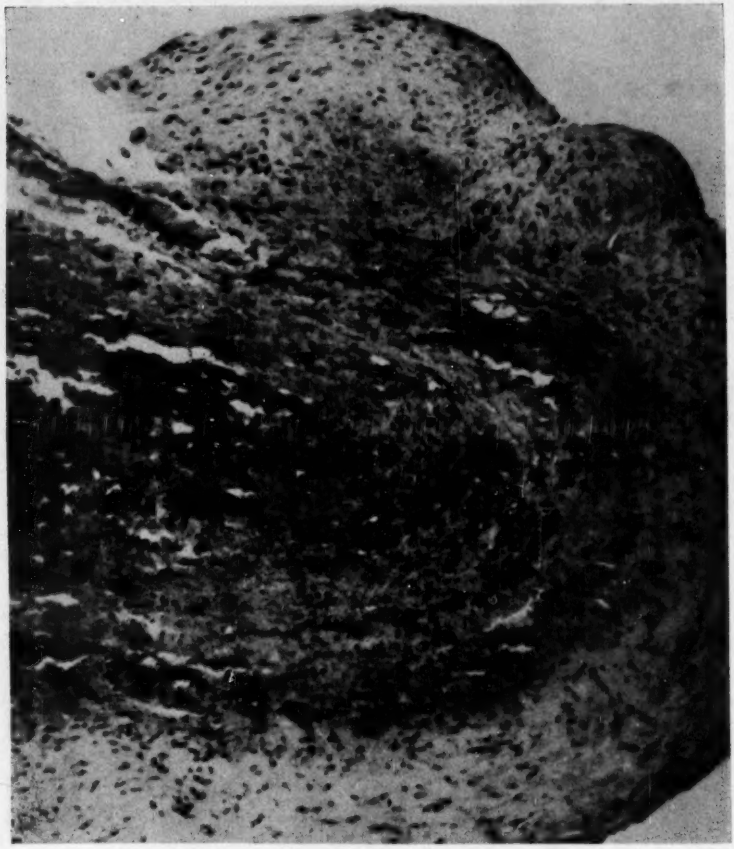

Fig. 9.—Microscopic section through lesion in figure 8.

was considerable blood loss, and transfusions were necessary. Microscopic section (fig. 5) revealed the wall to be thick, with a connective tissue reaction and little evidence of cleavage lines. This operation was difficult, while that in the former case was relatively simple.

The next case is that of a 10 month old boy with a history of a tumor in the neck which was first noted three weeks previously (fig. 6). The growth was easily removed, the sac showing a relatively thick wall with little secondary reac-

tion (fig. 7). Contrast this with a section (fig. 8) from a lesion in a 33 year old man, which had been present for 20 years. The removal of this hygroma was also difficult and hazardous.

A 15 month old boy had a known tumor for only three months. Unfortunately, acute inflammation developed in the mass six weeks prior to his admission to the hospital. This was treated by aspiration and chemotherapy. The residuals of the infection greatly increased the difficulty of excision of this tumor. Figure 9 is a microscopic section through this lesion. Again, delay, even though of short duration, complicated management and gave time for the infection to develop.

SUMMARY

We have endeavored to present a brief review of the modern concepts pertaining to the development and growth of cystic hygromas of the neck. The pathologic process and the methods of management have been discussed. Remarks relative to the eight patients who have been treated in the past four years have been included. It is our opinion that surgical excision of cystic hygromas of the neck is the treatment of choice. We have made a special effort to illustrate by cases presented the vital importance of early recognition and prompt removal of these tumors in order to prevent complications and recurrence.

DISCUSSION

DR. ARKELL M. VAUGHN, Chicago: I am interested in this subject because in 1931 I came into contact for the first time with the condition in a child who had a cyst on the right side of the neck almost as large as his head. He was operated on early, at the age of 2 months.

In going over the literature I discovered that in 1914 Dowd had tabulated 91 cases, and according to his report Radenbacker had reported the first case in 1828. I compiled 64 cases, which were published in the *American Journal of Diseases of Children* in July 1934. Since then the number of reported cases has increased considerably. The treatment at that time was surgical removal. I do not think the treatment has changed in the last 20 years.

I should like to ask Dr. Kibler if he knows how many cases have been reported up to the present time.

DR. FRANCIS KIBLER, Colorado Springs, Colo.: In answer to Dr. Vaughn, I have no idea how many cases have been reported to this time. My own experience with one case in the past six years does not allow me to comment.

CRITICAL ANALYSIS OF GOITER MANAGEMENT AT THE UNIVERSITY OF NEBRASKA HOSPITAL

GEORGE H. PESTER, M.D.
AND
HERBERT H. DAVIS, M.D.
OMAHA

DURING the past few years, numerous reports regarding the efficiency of the antithyroid drugs and of radioactive iodine in the treatment of toxic goiter have appeared in the literature. Other reports indicate that carcinoma of the thyroid in nodular goiter is much commoner than it was formerly appreciated. The present study was undertaken to evaluate objectively the results of treatment of goiter by various methods at the University of Nebraska Hospital during the past 15 years. The hospital does not maintain a goiter clinic and the results of goiter treatment represent averages obtained by a group of physicians associated with a teaching hospital.

The case histories of 670 patients admitted to this hospital from 1935 through 1949 with the diagnosis of goiter were critically reviewed, and follow-up studies were done. An accurate follow-up was possible in 71.8 per cent of the goiter patients. The 670 goiters were grouped as indicated in table 1.

The toxic cases were classified as follows: Patients with a basal metabolic rate of + 60 per cent or more on admission were considered as having severely toxic goiters; those with a rate from + 20 to + 59 per cent were considered to have moderately toxic goiters, and those with a rate below + 20 per cent but presenting toxic symptoms were considered to have borderline toxic goiters. The toxic cases were grouped as indicated in table 2.

MEDICAL TREATMENT

Sixty-four (15 per cent) of the toxic goiters were treated on the medical service. Only 10 of these were treated exclusively with antithyroid drugs, and the results are known in seven cases. Two patients (28.6 per cent) reported permanent remissions since discontinuance of the medication, one five years later and the other two and a half years later. Three have continued to be improved but are still taking the drug; one five years later, one three years later and the other one and one-half years later. One patient has had recurrence of symptoms since stopping the medication, and she now requests more treatment. The other patient reported that she had no improvement while taking the medication, but the adequacy of treatment since dismissal is not known. Reports from goiter clinics in

From the Department of Surgery, University of Nebraska College of Medicine.

larger centers indicate that about 52 per cent of the patients treated with antithyroid drugs will show permanent remissions after discontinuance of the therapy [1] (table 3).

The other 54 patients treated on the medical service had no therapy other than bed rest, sedation and perhaps a trial of strong iodine solution, U. S. P. The present status of 33 of these patients is now known. Eighteen (54.6 per cent) reported that they were improved, three (9.1 per cent) stated that they were unchanged, four (12.1 per cent) have undergone operation since their dismissal and eight (24.2 per cent) have since died and the course of the goiter is not known.

TABLE 1.—*Data on 670 Goiters (1935 to 1949)*

	Cases	%
Diffuse toxic	218	32.5
Nodular toxic	185	27.7
Nontoxic	199	29.7
Carcinoma	18	2.7
Recurrent	21	3.1
Persistent	12	1.8
Thyroiditis	17	2.5

TABLE 2.—*Cases of Toxic Goiter (1935 to 1949)*

	Cases	%
Diffuse, severe	49	7.3
Diffuse, moderate	134	20.0
Diffuse, borderline	35	5.2
Total Diffuse	218	32.5
Nodular, severe	20	3.0
Nodular, moderate	117	17.5
Nodular, borderline	48	7.2
Total Nodular	185	27.7
Recurrent	22	3.3
Total	425	63.3

SURGICAL TREATMENT

Three hundred and thirty-nine (80 per cent) of the toxic goiters were treated by surgical intervention, and the result is known in 227 cases. One hundred and

1. (*a*) Astwood, E. B.: Thiouracil Treatment in Hyperthyroidism, J. Clin. Endocrinol. **4**:229-248 (June) 1944. (*b*) Rose, E., and McConnell, J.: Thiouracil in the Treatment of Thyrotoxicosis: Clinical Experience with 37 Cases, Am. J. M. Sc. **208**:561-576 (Nov.) 1944. (*c*) Barr, D. P., and Schorr, E.: Observations on the Treatment of Graves' Disease with Thiouracil, Ann. Int. Med. **23**:754-778 (Nov.) 1945. (*d*) Fishberg, E. H., and Vorzimer, J.: Extrathyroid Effects of Thiouracil Therapy, J. A. M. A. **128**:915-921 (July 28) 1945. (*e*) Williams, R. H.: Thiouracil Treatment of Thyrotoxicosis: I. The Results of Prolonged Treatment, J. Clin. Endocrinol. **6**:1-22 (Jan.) 1946. (*f*) Bartels, E. C.: Thiouracil: Remission or Relapse of Hyperthyroidism After Discontinuing Its Use, Am. J. Med. **2**:150-155 (Feb.) 1947. (*g*) Aranow, H., Jr.; Elliott, R. H. E., Jr.; Frantz, V. K.; Melcher, G. W., Jr., and Werner, S. C.: Thiouracil in the Treatment of Thyrotoxicosis, Ann. Surg. **124**:167-179 (Aug.) 1946. (*h*) Fowler, E. F., and Cole, W. H.: The Advantages and Limitations of Thiouracil Therapy in Thyrotoxicosis, Surg., Gynec. & Obst. **84**:350-354 (March) 1947. (*i*) Greenberg, S. U., and Bruger, M.: Observations on the Prolonged Medical Management of Toxic Diffuse Goiter with Thiouracil and Propylthiouracil, Am. J. M. Sc. **220**:373-379 (Oct.) 1950.

ninety-seven (86.9 per cent) patients reported that they were cured or improved, 11 (4.8 per cent) had recurrence of their disease, 8 (3.5 per cent) had persistence of symptoms, and 11 (4.8 per cent) have since died and the result of the operation is not known.

One hundred and twenty-three (59 per cent) of the nontoxic goiters were treated by surgical intervention, and the result is known in 90 cases. Eighty-one patients (90 per cent) reported satisfactory results, three (3.3 per cent) had recurrence of the goiter, one (1.1 per cent) reported he was unchanged and five (5.6 per cent) have since died and the result of the operation is not known.

In all, 475 patients were treated surgically, and there were 14 deaths, a mortality of 3 per cent. Eight died in crisis, the last in 1941. Three died from postoperative pneumonia, the last in 1942. The other three deaths were due to technic, a technical mortality of 0.6 per cent. A substernal extension of a nodular goiter was left behind in two cases, and the patients died from respiratory obstruction. The other death was caused by bilateral recurrent nerve injury. Since the advent of the antithyroid drugs and the antibiotics, deaths from crisis and pneumonia are now almost nonexistent.

TABLE 3.—*Remissions After Withdrawal of Antithyroid Drugs*

Author	No. of Cases	Remission	
		No.	%
Astwood [1a]	18	9	50
Rose and McConnell [1b]	21	8	38
Barr and Shorr [1c]	47	36	77
Fishberg and Vorzimer [1d]	41	16	39
Williams [1e]	100	49	49
Bartels [1f]	21	8	38
Aranow and others [1g]	33	12	36
Fowler and Cole [1h]	19	9	47
Greenberg and Bruger [1i]	39	30	77
Total	339	177	52

ROENTGENOLOGIC TREATMENT

Twelve (2.8 per cent) of the patients with toxic goiters were treated with deep roentgen therapy. Also, four patients of this series who had recurrence after operation were treated with roentgen therapy. Of 11 patients who answered our questionnaire, eight (72.7 per cent) reported satisfactory results, two (18.2 per cent) reported their condition as unchanged and one (9.1 per cent) reported recurrence of his disease.

RADIOACTIVE IODINE

Ten (2.4 per cent) of the toxic goiters were treated with radioactive iodine. Six were toxic diffuse goiters, two were toxic nodular goiters and two were recurrent toxic goiters following surgical intervention elsewhere. The two nodular goiters were treated with radioactive iodine because of severe cardiac decompensation which made the patients poor risks for surgical treatment. In addition to the above 10 patients, three of this series who had recurrence after operation were also treated with radioactive iodine.

Twelve (92.3 per cent) of the 13 patients treated with radioactive iodine reported satisfactory results. One of the patients with a toxic nodular goiter reported that he was unchanged.

Reports from larger goiter centers indicate that radioactive iodine is effective in producing lasting permanent remissions in 94 per cent of the toxic patients treated [2] (table 4).

CARCINOMA AND NODULAR GOITERS

There were 18 cases of carcinoma of the thyroid in this series, an incidence of 2.7 per cent. In 13 cases the goiter presented a single nodule, in two cases there were multiple nodules, in one case the goiter was diffuse and in two cases there was no evident goiter.

Thirteen patients have died from their carcinoma, and five (27.8 per cent) are still living and well four to 15 years since leaving the hospital. The carcinoma consisted of a single nodule in four of the five patients still living; in three of these a subtotal thyroidectomy was done, and in the fourth case only the nodule was excised. The fifth patient still living is one who had undergone a laryngectomy for carcinoma of the larynx; when the specimen was examined microscopically,

TABLE 4.—*Radioactive Iodine Therapy of Toxic Diffuse Goiter*

Author	Year	No. of Cases	Cure	
			No.	%
Hamilton and Lawrence [2a]	1942	3	2	67
Herts and Roberts [2b]	1946	23	20	86
Chapman and others [2c]	1948	65	57	87
Moe and others [2d]	1950	100	100	100
Gordon [2e]	1950	135	135	100
Jaffe [2f]	1950	148	132	89
	....	----	----	---
Total	....	474	446	94

a primary carcinoma of the thyroid was also found. Johnson [3] found two primary carcinomas of the thyroid in 165 thyroid glands removed at necropsy in patients who died from diseases unrelated to the thyroid.

Of the 126 patients presenting a single nodule in which the nodule was examined microscopically, 12 (9.5 per cent) were found to have carcinoma of the thyroid. Of the 69 with nontoxic goiters, nine (13.1 per cent) had carcinoma. Three

2. (*a*) Hamilton, J. G., and Lawrence, J. H.: Recent Clinical Developments in the Therapeutic Application of Radio-Phosphorous and Radio-Iodine, J. Clin. Invest. **21**:624 (Sept.) 1942. (*b*) Hertz, S., and Roberts, A.: Radioactive Iodine in the Study of Thyroid Physiology: VII. The Use of Radioactive Iodine Therapy in Hyperthyroidism, J. A. M. A. **131**:81-86 (May 11) 1946. (*c*) Chapman, E. M.; Skanse, B. N., and Evans, R. D.: Treatment of Hyperthyroidism with Radioactive Iodine, Radiology **51**:558-563 (Oct.) 1948. (*d*) Moe, R. H.; Adams, E. E.; Rule, J. H.; Moore, M. C.; Kearns, J. E., Jr., and Clark, D. E.: An Evaluation of Radioactive Iodine in the Treatment of Hyperthyroidism, J. Clin. Endocrinol. **10**:1022-1028 (Sept.) 1950. (*e*) Gordon, E. S., in discussion on Treatment of Graves' Disease with Radioactive Iodine, at the Annual Meeting of the American Goiter Association, Houston, Texas, March 9-11, 1950. (*f*) Jaffe, H. L.: Radioiodine in the Diagnosis and Treatment of Thyroid Disease, Ann. West. Med. & Surg. **4**:272-273 (June) 1950.

3. Johnson, J. R.: Adenomatous Goiters With and Without Hyperthyroidism: Some Aspects of the Relationship of the Microscopic Appearance to Hyperthyroidism, Arch. Surg. **59**:1088-1099 (Nov.) 1949.

(5.4 per cent) of 57 toxic goiters presented single nodules which were toxic. Carcinoma was found in two of 128 goiters with multiple nodules, or 1.6 per cent. Both of these were nontoxic, an incidence of 4.5 per cent of all nontoxic multinodular goiters. There were no cases of carcinoma in toxic goiters containing more than one nodule. In all, there were 14 cases of carcinoma of the thyroid in 254 cases of nodular goiter, an incidence of 5.4 per cent (table 5).

SUMMARY AND CONCLUSIONS

All cases of goiter (670) observed at the University of Nebraska Hospital during the past 15 years were critically reviewed and classified.

In cases of toxic goiter, lasting remissions were produced by surgical treatment in 86.9 per cent of the patients treated, by radioactive iodine in 92.3 per cent, by roentgen therapy in 72.7 per cent and by antithyroid drugs in 28.6 per cent. Reports from the literature indicate that about 52 per cent of patients with toxic goiter treated with antithyroid drugs have lasting remissions after discontinuance of the medication.

TABLE 5.—*Carcinoma and Nodular Goiters Proved Microscopically*

	No. Operated on	Cases of Carcinoma	%
Single nodules	126	12	9.5
Nontoxic	69	9	13.1
Toxic	57	3	5.4
Multiple nodules	128	2	1.6
Nontoxic	44	2	4.5
Toxic	84	0	0.0
Total	254	14	5.4

There were three deaths due to technic in 475 patients treated surgically, a technical mortality of 0.6 per cent. There have been no surgical deaths from crisis since 1941 and no deaths from postoperative pneumonia since 1942.

On the basis of the findings of this study, it is much safer to remove a nodular goiter surgically than to let it go unattended. The operative mortality of 0.6 per cent is much lower than the incidence of carcinoma in nodular goiter. Primary carcinoma of the thyroid was found in 13.1 per cent of the nontoxic goiters presenting a single nodule and in 9.5 per cent of all goiters presenting a single nodule. Carcinoma was found in 5.4 per cent of all nodular goiters examined microscopically. There were no cases of carcinoma in toxic goiters containing more than one nodule.

DISCUSSION

DR. CLAUDE J. HUNT, Kansas City, Mo.: Dr. Pester has made a critical analysis of a fairly large group of cases. I think it is timely that this subject be presented before the Association. There are many controversial problems relating to it, and it is particularly timely during the presidency of Dr. Cole, who has contributed so much to our knowledge referable to the relationship of malignant processes to thyroid pathology.

With the advent of the antithyroid drugs, it was natural that many persons would think that patients with hyperthyroidism could be treated indefinitely with antithyroid medication and that surgical intervention would be unnecessary. In this report by Dr. Pester and Dr. Davis the relative percentage of patients who were successfully treated for a period on antithyroid drugs, with permanent remission for three and a half to five years, was only 28.6.

On the basis of reports from large clinics, I believe the highest percentage is about 52 per cent of patients who can be carried along for a period and then remain in a relative state of remission after the medication has been stopped. That percentage is relatively low when compared with the benefits that can be obtained by surgical removal. When it is considered that surgery has advanced to the point at which the mortality rate is less than 1 per cent and surgical tragedies are relatively infrequent, it seems that it is preferable to resort to thyroidectomy when these patients are in normal metabolic balance. Certainly it always should be performed in the presence of nodular goiter. Even though these patients are held in remission by antithyroid drugs, nothing has been done to the nodule to prevent it from progressing, with some of the complications that we recognize so frequently associated with this type of goiter.

There are some instances, perhaps, when antithyroid medication should be continued. I refer to patients who have had serious nerve injury on one side from a previous operation, and a preponderance of recurrence on the opposite side. I think the hazard of surgical intervention then might possibly justify one continuing with the antithyroid drugs if medication seemed to be adequate.

In regard to young persons who are approaching the age of puberty with a moderate hyperthyroidism, I think it is well to carry them along for a time until some degree of adolescence develops before surgical treatment is employed. We have under observation now three girls of about that age group whom we have kept in remission for a period of two or three years by this method, and they have got along very well. This policy, however, is controversial and probably should be only occasionally pursued. It is not justifiable if there is a discrete nodule associated with the hyperthyroidism.

The problem of radioactive iodine is also a controversial one. There are some prominent physicians in this country, heads of large surgical clinics, who are using radioactive iodine rather generally in primary hyperthyroidism. They are getting excellent results. The report here shows 92 per cent, and the general report is 94 per cent. That is very good, but we do not know yet what the effects of radioactive iodine are. That will take several years to determine.

Personally, I do not want radioactive iodine used on myself, and one has to make a personal evaluation of it before one gives radioactive iodine to one's patients. Certainly it is not desirable in toxic nodular goiter, for the same reason that I mentioned relative to the antithyroid drugs.

There are some instances reported wherein radioactive iodine has been effective in metastatic carcinoma of the thyroid gland. After the thyroid gland itself has been removed there seems to be a tendency for the metastatic processes to take up thyroid function and to produce hormone, and in some instances these metastatic lesions have taken up the radioactive iodine. This substance, therefore, may be effective in the treatment of metastatic carcinoma. In some instances thyroid therapy has been instituted to stimulate these metastatic lesions to take up the radioactive iodine.

Certainly I would not want to give radioactive iodine to an adolescent, to a young man who is married and who expects to be a father or to a young woman of the childbearing age. Its use should be restricted to persons who are in the midperiod of life or later.

Dr. Cole has contributed so much to our knowledge of the relationship of cancer to nodular goiter that we have all become cancer conscious, and we now are finding cancers associated with nodular goiter that I am sure in years gone by were not recognized.

The high percentage of cancer associated with discrete nodular goiter makes it imperative that discrete nodules in the thyroid gland be removed, and the younger the patient the more likely they are to be associated with a malignant process. So frequently is cancer associated with any type of nodular goiter and so low is the mortality rate that all nodular goiters should be removed.

We have practiced removal for years. In recent years we have been finding more cancers associated with nodular goiter than we had previously. I am sure that is because we have become more cancer conscious and have been looking for them. In the past year we have found three cancers in discrete nodules in young women, all less than 23 years of age.

Surgical intervention for cancer of the thyroid should be on the same basis as that for cancer elsewhere. The primary lesion and all gland-bearing tissue should be removed. In

other words, I do not think it is sufficient just to take out the nodule or to do a complete lobectomy with removal of the isthmus on that side and leave the lymphatic glands unremoved. I think there should be a radical neck dissection.

As proof of that I wish to cite the case of a prominent lawyer in our community, who in 1932 underwent a subtotal thyroidectomy on the left side for a nodule in the thyroid gland. No dissection of the neck was done and no further operative procedure. He was given the usual roentgen treatment of that time.

He remained well until 1945, when he consulted us. He had recurrent nodules in the neck, and a radical dissection of his neck was done, with vein excision. Glands of a malignant nature were found. He remained well until 1949, and then he returned, unable to breathe or swallow. It was necessary to perform tracheotomy and a gastrostomy. He lived for a few weeks and then died.

I think this case exemplifies the necessity of approaching cancer of the thyroid gland by the same radical means that we approach cancer of the breast or cancer elsewhere, namely, a total removal of that lobe, removal of the isthmus and dissection of the glands of the neck. I believe that if this man had had that treatment at the first operation he might not have died from extension of the recurrent cancer into vital structures such as the trachea and the esophagus.

Dr. Warren H. Cole, Chicago: Dr. Davis reported that 87 per cent of his patients who underwent thyroidectomy were cured or improved and that 4.8 per cent had recurrence of symptoms. These figures correspond closely to the experience of others, including our own. His figure of 92 per cent good results following use of radioactive iodine is slightly better than that reported in the literature, but, as he stated, his series in that group was small. All of us are intensely interested in the possibility of utilizing radioactive iodine in hyperthyroidism. At first I was optimistic about the use of this drug, thinking that it would eliminate thyroidectomy in the great majority of cases. However, I am becoming less convinced of its value for universal use.

Perusal of data assembled by the late Dr. Soley indicates that in 288 cases good results were obtained in 83 per cent. In this series 8.5 per cent had hypothyroidism or myxedema. There was great difficulty in determining dosage. Soley reported that it varies between 23 and 575 micrograms per gram of thyroid. The average duration of treatment until euthyroidism was obtained was five months. The danger of transformation to carcinoma seems significant because radioautographic studies have revealed collection of radioactive iodine in innumerable fine deposits throughout the gland. All workers agree that this substance should not be given to young persons.

I was not sure whether Dr. Davis always utilized propylthiouracil to bring the patient to a euthyroid state before thyroidectomy was performed. Personally, I am convinced that the postoperative mortality rate following thyroidectomy will be lower if we perform thyroidectomy only after all hyperthyroidism has been obliterated but before hypothyroidism develops. Data recently assembled by Dr. Fowler in our clinic indicates that the combined mortality rate following thyroidectomy for toxic diffuse and toxic nodular goiter was 1.03 per cent for the period 1936 to 1944, before the use of antithyroid drugs. By coincidence the mortality rate in nontoxic nodular goiter was identical, namely, 1.04 per cent. Since 1944, when thiouracil was introduced in our clinic we have not had any deaths, although we have performed only 316 thyroidectomies. Since the mortality rate after thyroidectomy for toxic goiter is so low, the figures which I have just given you are scarcely sufficient in number to reflect truly the comparative mortality rates in the two series. However, we make it a point in our clinic to bring the basal metabolic rate down to near zero with propylthiouracil and give iodine for the last two weeks, with omission of propylthiouracil for four or five days just preceding thyroidectomy.

Dr. George H. Pester, Omaha: In answer to Dr. Cole, Dr. Davis and I feel that the patients with the milder forms of hyperthyroidism should be given first a course of strong iodine solution; if a prompt response is not obtained, then they are given antithyroid drugs. After the hyperthyroidism has been controlled adequately, operation is performed. In this series, 14 patients with toxic goiter were treated preoperatively with the antithyroid drugs. There were no deaths in this group, and every patient had an uneventful convalescence.

MIKULICZ'S DISEASE

A Report of Two Cases

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TRUE Mikulicz's disease is rare. Few surgeons have ever had a case. A search of 10 standard surgical textbooks revealed no mention of the disease, yet its cure may require surgical intervention. Less than 100 authentic cases were found in the literature, although the latter is replete with cases that do not fit the classical description of the disease given by Mikulicz before the society for scientific medicine at Königsberg in 1888.

Mikulicz said:

> Both lacrymal glands and all the salivary glands were changed in a symmetrical manner into tumors, which pushed themselves markedly forward from the normal position of these organs and thereby distorted the physiognomy of the patient in a remarkable way. The tumors had arisen gradually; they were at the time of examination of a hard consistency, painless, without trace of inflammatory signs. Moreover, elsewhere there were present no pathological changes in the bearer of these tumors. . . . Seven months previously, in June 1887, he noticed that both upper eyelids began to swell; he had no pain or other trouble. . . . Later the palpebral fissure became so narrowed that it was difficult for him to see. Soon afterward there appeared under both angles of the jaw, similar painless swellings, which as they grew larger, interfered with eating and speaking. . . . In the blood there is no striking change, especially no leukocytosis. . . . The countenance appears strikingly altered because of the symmetrical swelling in the region of the upper eyelids, the parotid and the submaxillary glands. The upper eyelids hang down so far, especially in their outer halves, that the palpebral fissure is reduced to a narrow, triangular space, with base formed by the inner two-thirds of the lower lid. . . . The patient is unable perceptibly to raise the upper lid himself, even with strong effort. . . . Under each angle of the jaw projects a tumor about the size of a hen's egg, covered by a normal, moveable skin. . . . If the patient opens his mouth, attention is drawn at once to tumors corresponding to the two sublingual glands. . . . During the examination, a copious secretion of saliva takes place, but there is otherwise no sign of salivation existing.

This detailed description of the disease, which has been named after the surgeon who so clearly portrayed it, like many classical descriptions, has never been improved on. The powers of observation of scientists of past generations seems to have been more highly developed and their descriptions more minute and painstaking.

From a study of the literature it is obvious that some authors either were not familiar with this classical description or they thought it covered a multitude of conditions. Consequently, many diseases such as tuberculosis, syphilis and leukemia have been reported under Mikulicz's syndrome. As a result, much confusion has arisen regarding both the diagnosis and the treatment of this condition. Obviously,

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From the Jackson Clinic.

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 2, 1950.

cases including an abnormal blood picture, as in leukemia, and those including changes in the lymphatic glands, as in tuberculosis, should not be included. Involvement of the lacrimal and salivary glands may occur in leukemia but as such is merely a local manifestation of a general blood disease.

The etiology of this disease remains unknown. Mikulicz believed that he was dealing with an infectious disease, and no one has disproved this theory. The fact that my first patient responded favorably to penicillin and did not require surgical treatment, as did my second patient, would seem to substantiate the claim. It is possible that the disease may extend from the salivary to the lacrimal glands by way of the nasolacrimal duct, since the mucous membrane of the mouth is continuous with that of the conjunctival sac. The conjunctivitis noted in my first patient would seem to corroborate this original idea of Mikulicz. Fever, however, is not characteristic but has occasionally been reported to have occurred.

The disease may occur at any age but is most common in early adult life or in middle age. It is slightly more prevalent in males. My two patients, although differing considerably in appearance, nevertheless presented a characteristic triad of symptoms that should easily and quickly enable one to establish a diagnosis of this rare condition. The peculiar appearance of the face, with narrowed palpebral fissures, the symmetrical enlargement of the salivary glands and the parchment-like dryness of the tongue were typical of Mikulicz's description.

Strangely enough, in contrast to most other diseases of the neck and mouth, the general health of the patient is good. The lack of saliva, however, is annoying and causes considerable discomfort in the matter of masticating, swallowing and singing.

The prognosis is variable. In some of the cases reported in the literature the disease persisted for months or even years, with periods of remission, and then finally subsided. Various methods of treatment have been advocated, namely, surgical treatment, roentgen therapy, and administration of iodides. The patients whose cases are reported here are the first to have received penicillin. I have found no report of sulfonamides having been tried. They were used unsuccessfully in my first case before I saw the patient. Reports of patients treated successfully by roentgen therapy have been made by Pfeiffer, Evans and Leucutia, Hodges, Wright, Hamilton, Pohle, and Miller and Eusterman. Two patients were successfully treated with radium by Pinch.

The pathological picture is typical, the true glandular tissue being replaced by lymphocytes, either in section or throughout the whole section. Connective tissue may be marked in some cases and is probably an indication of a more advanced state. The process appears to represent a chronic inflammatory state, although it is believed by some observers to be indicative of a benign neoplasm. Boyd is of the opinion that the condition may be regarded as a localized form of lymphoblastoma.

REPORT OF CASES

CASE 1.—Mr. C. M., aged 52, came to the Jackson Clinic on Aug. 21, 1944, complaining of extreme dryness of the mouth and lumps in his neck, which he had first noted three weeks previously. He thought it had begun when he yawned and the muscles of his neck seemed to tighten. The following day he noticed that the glands of his neck were swollen, and he called his local physician, who gave him a sulfonamide drug, with no apparent improvement. Two weeks prior to his coming to the clinic the saliva stopped flowing, and he consulted other physicians, who tried various remedies such as hypodermic injections, electric treatments and

mouth washes, without success. The swelling of the glands increased to such an extent that he found it difficult to open his mouth; his eyes were nearly swollen shut, and his voice likewise was affected.

On examination, the general physical findings were normal except for the following conditions. There was a rather marked enlargement of the sublingual, submaxillary and parotid glands. The enlargements were smooth and not tender but sufficiently large to interfere with speaking and eating. There was symmetrical swelling in the region of the upper eyelids, which hung down so far, especially in their outer halves, that the palpebral fissure was reduced to

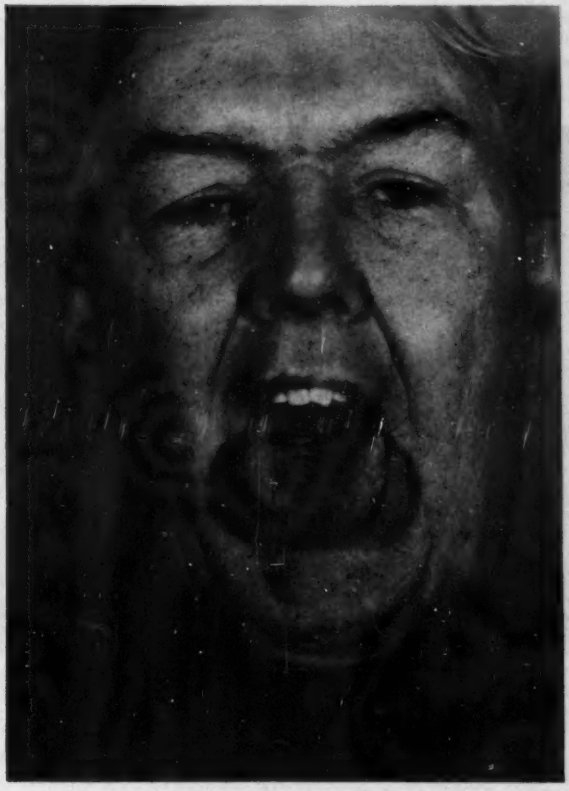

Fig. 1 (Case 1).—Typical appearance of patient with Mikulicz's disease. Note the parchment-like dryness of the tongue, the swelling of the salivary glands and the narrowing of the palpebral fissures.

a narrow triangular space with the base formed by the inner two thirds of the lower lid. The patient was unable perceptibly to raise the upper lids himself even with strong effort.

On the first examination the patient was able to open his mouth only enough for the tongue to be seen with some difficulty, but after a few days' treatment he was able to open it sufficiently so that one could see the tongue, which revealed the parched dryness characteristic of Mikulicz's disease. His voice had a husky note. He said that because of the dryness of his entire mouth his diet was almost entirely liquid. His temperature was 99.6 F. Urinalysis showed a specific

gravity of 1.010, an acid reaction, no sugar and a few red blood cells. The hemoglobin content was 81 per cent, and erythrocytes numbered 3,990,000 and leukocytes 10,550, with 15 lymphocytes, 4 large mononuclear cells, 3 transitional cells, 76 neutrophils, and 2 eosinophils. Roentgenograms of the parotid and submaxillary areas revealed no evidence of salivary calculi.

The complete picture suggested an acute stage of Mikulicz's disease with the typical enlargement of the salivary glands, absence of saliva, conjunctivitis, narrowing of the palpebral fissures, painless, nontender glands, which were firm and smooth and not adherent to the surrounding structures, and ptosis of the eyelids. His general health was good except that he found it impossible to masticate.

A review of the literature revealed that there was considerable conjecture regarding the classification of cases of true Mikulicz disease and those considered under the Mikulicz syndrome. Some cases had responded to surgical treatment and others to roentgen therapy. I was unable to find a report on any patient successfully treated with sulfonamides. Although

Fig. 2 (Case 2).—*A*, preoperative view showing enlargement of salivary glands, especially the submaxillary glands, in a case of true Mikulicz disease. *B*, same patient after surgical removal of submaxillary tumors.

the etiology of the disease has remained a mystery, in many ways it suggests a low grade infection of the salivary ducts. Therefore, it was decided to try penicillin therapy. The patient was given 100,000 units diluted with 20 cc. of sterile isotonic sodium chloride solution. He was given 5,000 units per cubic centimeter concentration each 24 hours, the dosage being 2 cc. intramuscularly every three hours night and day for 72 hours. Treatment was started on August 22, and on August 25 the patient noted that saliva began to flow and that the glands were rapidly receding. He was able to open his mouth wider, could eat solid food, and could chew meat for the first time in four weeks. The conjunctivitis was receding also. In view of the mild secondary anemia which was present, he was given powdered stomach (kapseals ventriculin®) with iron and vitamin B capsules, one three times daily.

On September 5 it was noted that the salivary glands were nearly normal in size, and there was a further improvement in the eyes, but the tongue seemed drier. The patient was readmitted to the hospital and was given another 100,000 units of penicillin. On September 9 his condition

generally seemed to be improved, but it was noted that there appeared to be a cycle of three or four days' duration when the tongue was dry and then became moist again. Further improvement of the eyes was noted, and he no longer complained of a burning sensation. Because of the intermittent flow of saliva, it was decided that he be given a course of radium over the region of the left salivary glands. He was given a dosage of 350 mg.-hr. over two areas and was to return for further treatment of the right salivary gland area in three weeks but reported that he had so sufficiently improved that he did not think it necessary.

It is not possible to say conclusively that penicillin effected a cure in this case, as sufficient time had not elapsed before the use of radium. It is certain that the swelling of all the salivary glands and the conjunctivitis had subsided before radium was used and that the flow of saliva had commenced so that he was able to open his mouth fully and properly masticate solid food.

On November 2 the patient reported that the flow of saliva was normal except when he awakened in the morning, that his eyes had entirely cleared up and that he was working six days a week and feeling well. He was able to eat a steak and enjoy it. He had rejoined his singing group and was able to carry on normally in this respect.

Fig. 3.—Photomicrograph showing replacement of glandular tissue by lymphoid tissue in tumors removed from patient in figure 2.

CASE 2.—Mrs. A. S., aged 40, came to the Jackson Clinic on Jan. 1, 1950, because of bilateral, painless swellings in the neck and dryness of the mouth and tongue. While there was marked swelling of the submaxillary glands, it was less noticeable in the lacrimal glands. She stated that the glands had gradually enlarged during the previous three weeks. The eyelids had become slightly swollen.

On examination, bilateral tumors were noted that were freely movable, not tender, and about the size of a hen's egg, just beneath the angle of the jaws in the sublingual gland region. The tongue was dry but not parched as in the previous case, and no salivary secretion was seen. The general physical examination was otherwise noncontributory save that it revealed the presence of slight adenopathy of the inguinal glands and bilateral varicose veins. The spleen was not enlarged. The temperature was normal, as were the differential count and other blood counts. Roentgen examination of the chest gave negative results. Thus, leukemia and Hodgkin's disease were not suggested, although the latter could not be ruled out without a biopsy.

Since the patient was nursing a baby and had three other children dependent on her, her husband being in the Army in Japan, it was decided to treat her with penicillin at home. This was tried but did not prove satisfactory because of inadequate dosage. The flow of saliva did increase, and some slight diminution in the size of the glands was observed. After two weeks surgical removal of the right submaxillary tumor was performed, and the pathological report by Dr. Etheldred L. Schafer was as follows:

"The specimen consists of an encapsulated, bosselated mass measuring 5.5 by 3.5 by 3 cm. It is entirely encapsulated by a thin, transparent, connective tissue capsule, which transmits the pale tan color of the underlying lobulated tissue. Section reveals slightly bulging, pale tan tissue which is distinctly divided into lobules. Microscopic section of different portions of the gland shows retention of the normal, lobulated structure of salivary gland. However, the lobules show marked replacement of glandular tissue by lymphoid tissue. In the lymphoid tissue, large, irregularly shaped, discrete, pale, secondary centers are prominent. These are surrounded by a rim of rather densely concentrated, small lymphocytes. The remaining salivary tissue is widely separated by these follicles. The glands are small but lined by normal epithelium. A few contain acidophilic masses within their lumens. There is diffuse infiltration of lymphocytes between the glands. An occasional eosinophil is identified. There is no evidence of neoplasia in these sections. The diagnosis is chronic sialadenitis consistent with the diagnosis of Mikulicz's disease of the salivary gland."

As no change occurred in the left submaxillary mass, this was also excised on May 10, 1950, and again the pathological report showed Mikulicz's disease. Convalescence was uneventful, and the patient gradually experienced a normal flow of saliva and normal health.

SUMMARY

Two cases of Mikulicz's disease are reported. In the first case the patient responded to penicillin therapy. The second patient did not respond to inadequate penicillin therapy, and the tumors were excised surgically. Heretofore, either surgical or roentgenologic treatment was used.

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DISCUSSION

DR. RAYMOND W. MCNEALY, Chicago: About six months ago I saw a case of Mikulicz's disease. I did not recognize it for a while because the patient came to me for a hernia repair. He was a dressy fellow who wore a rather tight collar and a pin under his tie. I noticed that his features hung over a little on the side. The rest of his body was not so heavy. On examining him I noticed that his submaxillary glands were enlarged and soft. I felt under his arms, thinking he might have Hodgkin's disease.

The man slowly improved without any particular medication. We had him take a few roentgen treatments, which I could not see had much influence at the time. The glands have shrunken somewhat, but the swelling is not entirely gone. He also has the narrowing palpebral fissure, but it does not interfere with his work. He looks just a bit "stuffy" above his collar for the size of his body. That was the thing that attracted my attention.

EXPERIMENTAL AND CLINICAL OBSERVATIONS ON RISING INTRACRANIAL PRESSURE

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CUSHING in 1901 stated: "The fact that cerebral compression occasions a rise in blood pressure is universally known but it does not seem to have been recognized that the degree of this elevation occurs *pari passu* with the degree of compression to which medullary centers are subjected." [1] He later elaborated clinically on this concept.[2] Although his experimental work demonstrated clearly that blood pressure elevation did not occur until high degrees of compression had developed, the application of the experimental concept to clinical problems inexplicably lost sight of this fact. In the next four decades it became widely accepted teaching that the clinical state produced by expanding intracranial lesions is characterized by a concomitant association among increased intracranial pressure, vascular hypertension and bradycardia, a triad of responses that has been termed the Cushing phenomenon. These changes in the vital signs are seen together so rarely in subjects with high intracranial pressure that they are of little use in the diagnosis and management of this disorder, as has been shown by the clinical and experimental studies of Browder and Meyers.[3] Nevertheless, these observations somehow have not lessened appreciably the pervasiveness of the Cushing doctrine.[4]

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 2, 1950.

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(Footnotes continued on next page)

Figure 1 is an illustration from Cushing's classic paper. It illustrates in the dog anesthetized with morphine and ether the absence of any appreciable vascular pressor response until the intracranial pressure approaches the blood pressure, the characteristic swings of the blood pressure about the mean intracranial pressure as the latter is further elevated and the associated bradycardia and apnea. In experiments designed to show the influence of changes in cerebral blood flow on intracranial pressure in rhesus monkeys anesthetized with pentobarbital sodium (nembutal®)[5] we have made extensive observations on the physiological responses induced by increases in intracranial pressure, including the Cushing phenomenon. We have observed the characteristic absence of any effect on blood pressure, heart

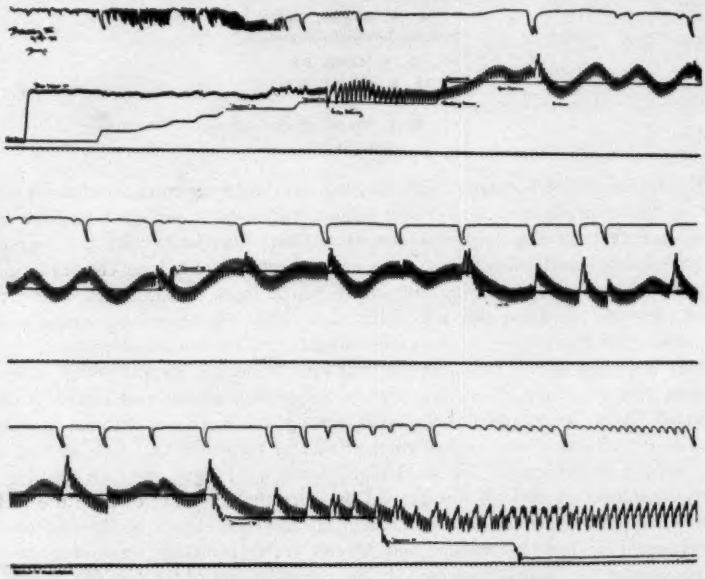

Fig. 1.—The association among respirations, arterial pressure and lumbar pressure in an anesthetized dog (after Cushing). The top line records respirations and the bottom line the time in two seconds intervals. The blood pressure is labeled by the pulse variations. The mean initial pressure is 114 mm. The intracranial pressure is the level of a reservoir in communication with the subarachnoid fluid space, referred to the level of the trephine opening in the skull. It is referred to the same base-line as the arterial pressure and also expressed in millimeters of mercury.

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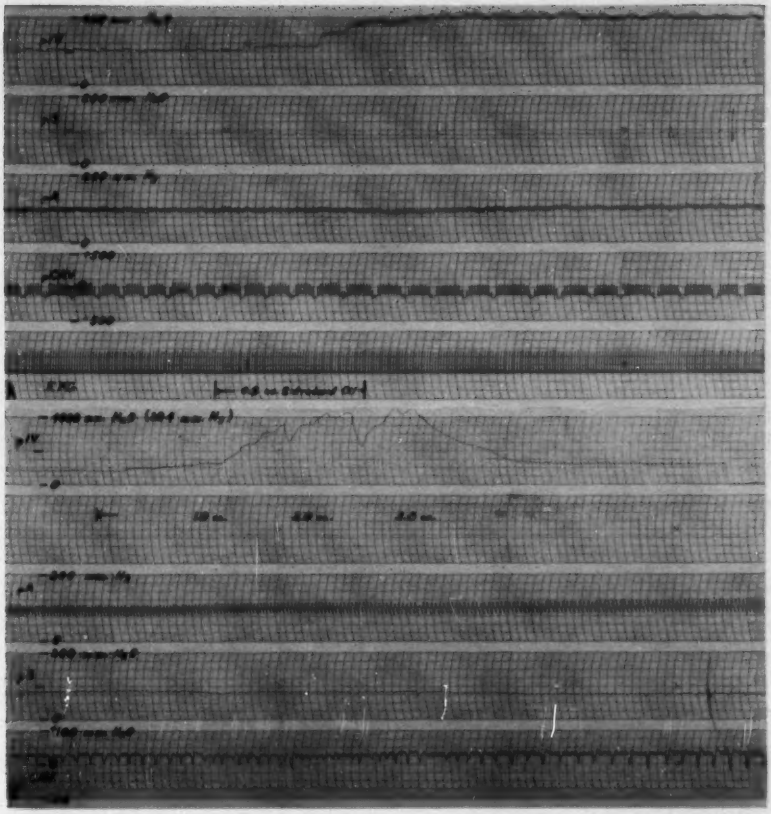

Fig. 2.—*A*, the pressure responses of an anesthetized monkey to the introduction of oil extradurally. The top line is the pressure at the tip of a needle in the lateral ventricle (*pIV*). The second line is the pressure at the tip of a catheter in the sigmoid sinus (*pS*). The third line is the pressure at the tip of a catheter in the femoral artery (*pA*). The fourth line is the pressure at the tip of a catheter in the superior vena cava (*pCAV*) and is under arterial influence. The fifth line is lead II of an electrocardiogram (*EKG*). On this and subsequent tracings the time interval marked by four vertical lines is five seconds. The method of recording pressures has been described.[2] *B*, the pressure responses of an anesthetized monkey to the introduction of oil intracranially. The pressures are the same as in *A*. In the second channel is shown the addition of oil. Note that the arterial pulses in *pIV* are absent when *pIV* is greater than 1,500 mm. of water (110 mm. of mercury, the systolic pressure).

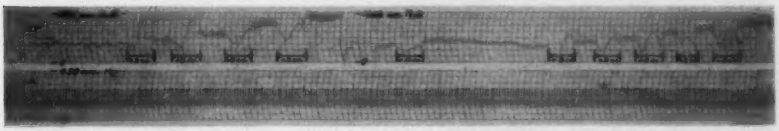

Fig. 3.—The relation between arterial and lumbar pressures of an unanesthetized subject several days after the evacuation of a chronic subdural hematoma. The top line is the pressure in a needle in the lumbar subarachnoid space (*pLP*). The bottom line is the pressure in a needle in the brachial artery (*pA*). The subject is lying on her side, and the pressures are referred to the level of the vertebral spines. *pLP* has no physiological meaning while fluid is being added as the transducer is not connected to the subarachnoid space.

rate or respiration of increases in intracranial pressure to less than the arterial pressure, induced by adding saline to the lumbar subarachnoid space or the lateral ventricles or by injecting oil extradurally or intracerebrally (fig. 2).

In man the addition of saline to the lumbar subarachnoid space or to the lateral ventricles causes a concomitant rise in the intraventricular and lumbar pressures

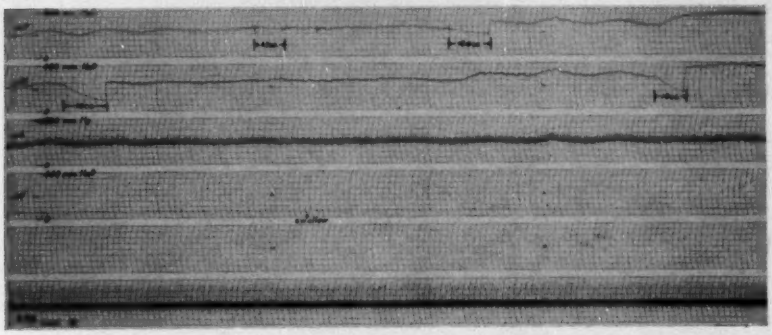

Fig. 4.—Correspondence among pressures of a comatose subject with an inoperable glioma. The top line is the pressure in a catheter in the lumbar subarachnoid space (*pLP*). The second line is the pressure in a catheter in the lateral ventricle (*pIV*). The third line is the pressure at the needle tip in the femoral artery (*pA*). The fourth line is the pressure in a needle in the right jugular bulb (*pJ*). The subject is lying on his back, and the pressures are referred to 10 cm. above the midback. The sixth line is lead II of the electrocardiogram (*EKG*).

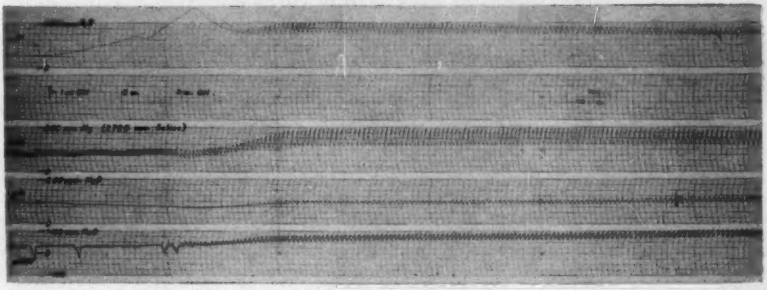

Fig. 5.—The pressure responses of an anesthetized monkey to the introduction of oil intracerebrally. The pressures are designated as in figure 2. The respirations are shown by the sudden drops in the caval pressure and disappear as the hypertension begins.

and also, with pressures near but not equal to the arterial pressure, induces no change in the arterial pressure, rate or depth of respirations, heart rate, jugular vein or superior vena cava pressures or the electrocardiogram (figs. 3 and 4). We will present elsewhere evidence that the reduction in cerebral flow occasioned by lowering the effective inflow pressure of blood into the brain by this maneuver is transient, being compensated for within seconds by active reflex dilatation of the cerebral arterioles.

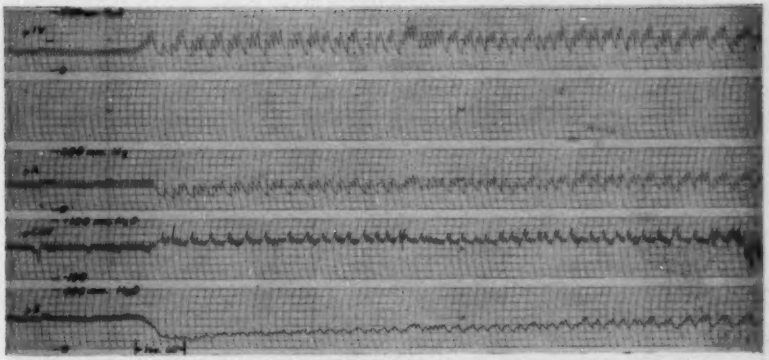

Fig. 6.—The pressure responses of an anesthetized monkey to the addition of oil extradurally. The top channel (ϕIV) records the pressure in the basal cistern. The other pressures are as in figure 2.

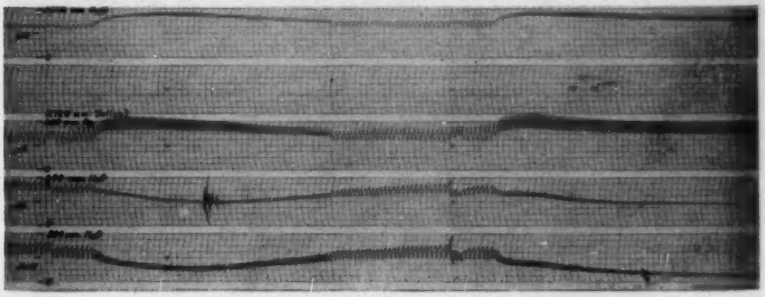

Fig. 7.—The pressure responses of the same monkey as that in figure 5 recorded three minutes later. There are transient artefacts in the down swings of the sinus and caval pressures.

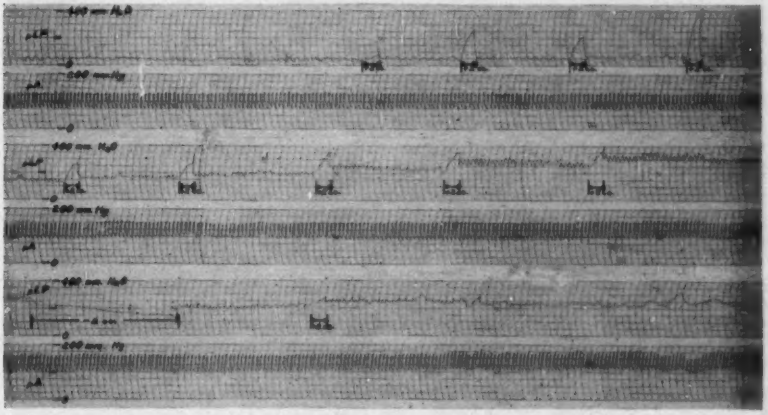

Fig. 8.—The pressure in the lumbar subarachnoid space and in the femoral artery in a conscious subject three days after a cranioplasty. The subject is lying on her side. The pressures and reference point are as in figure 3. The pair of tracings in the middle follows the top pair by 20 minutes. During the interim 20 cc. of fluid had been added. The pair of tracings in the bottom line follows directly after the middle pair.

In monkeys hypertension, bradycardia and apnea are usually induced together as the intracranial pressure is further elevated (fig. 5). Bradycardia may be induced alone with an associated hypotension (fig. 6). If hypertension occurs, the intracranial pressure rises further and the rise lasts as long as the vascular hypertension (fig. 7). It is nearly always associated with apnea but has not been induced

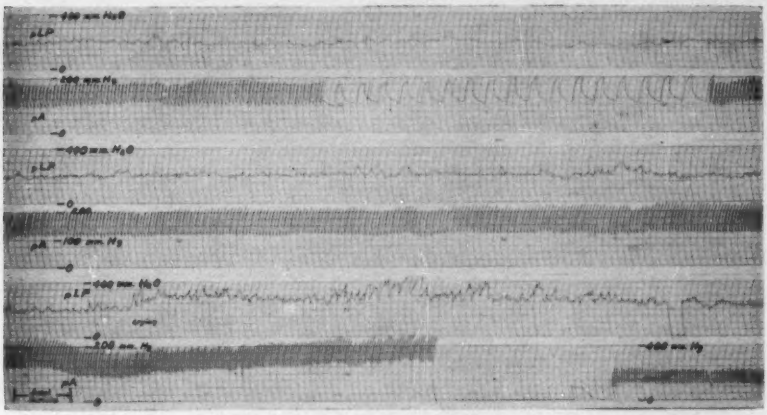

Fig. 9.—The pressure in the lumbar subarachnoid space and in the femoral artery in a conscious subject three days after a cranioplasty. These three pairs of tracings follow directly after those of figure 8. In the top pair of tracings the time interval represented by five vertical lines is one second during the period when the arterial pulses are more widely separated. The transducer recording the arterial pressure in the bottom pair of tracings is shifted to the ambient pressure in order to check on drift in the recording system and then attenuated.

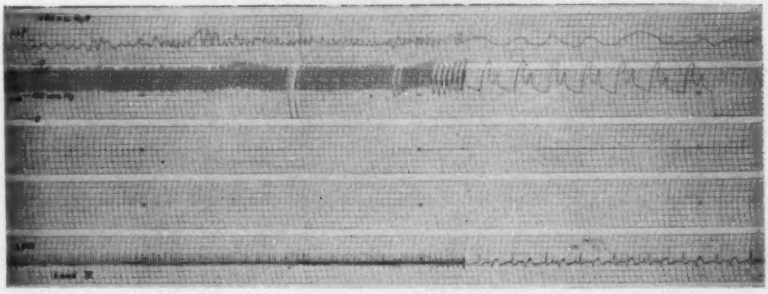

Fig. 10.—The pressure in the lumbar subarachnoid space and in the femoral artery in a conscious subject three days after a cranioplasty. This tracing follows 15 minutes after that in figure 9. Lead II of the electrocardiogram was recorded in the bottom line in order to show that the coupled beats in the arterial pressure are due to premature ventricular contractions.

by clamping the trachea. The association between the development of hypertension and the further rise in intracranial pressure was not observed by Cushing because in his experiments there was an open system; the subarachnoid fluid was connected to an extracranial reservoir which kept the intracranial pressure constant. We have adduced indirect evidence to show that the association here between the intracranial pressure and the arterial pressure is due to transmission of the arterial pressure

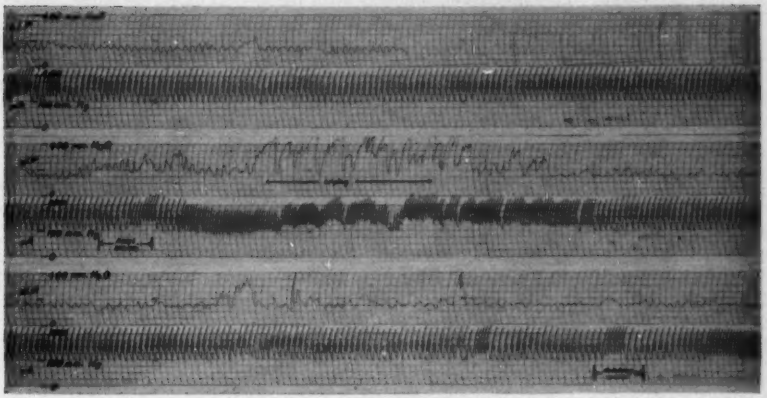

Fig. 11.—The pressure in the lumbar subarachnoid space and in the femoral artery in a conscious subject three days after a cranioplasty. These pairs of tracings follow two and a half minutes after those in figure 10. The lumbar pressure in the top line is interrupted by calibration of the transducer system to check on attenuation of the amplification with time.

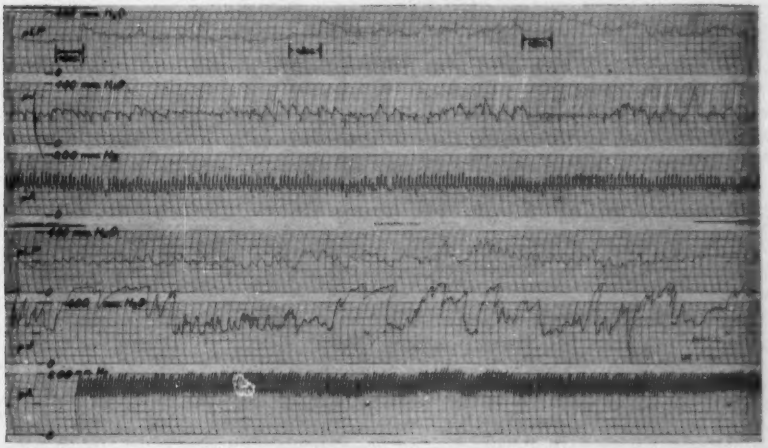

Fig. 12.—Pressures in a conscious subject with a left hemiparesis several days after a thrombosis of the right middle cerebral artery. The patient is lying on his side. The pressures are as in figure 3, with the pressure in the jugular bulb in channel 2. The top three tracings were recorded simultaneously sometime after the addition and withdrawal of small amounts of cerebrospinal fluid. All the pressures are distorted by hiccups at the rate of 27 per minute. The lower three tracings were taken 10 minutes later after 12 cc. more fluid had been added. The lumbar pressure had returned after the addition of this fluid to its previous level. The arterial pressure had risen gradually, and the hiccuping had disappeared. The internal jugular pressure, in particular, reflects the motion of the subject who had become restless and more confused.

farther down the intracranial vascular tree because of reflex dilatation of the cerebral arterioles. This dilatation, together with the rise in blood pressure, results both in a surge in cerebral blood flow and in an associated increase in intracranial volume, which latter change in turn raises the intracranial pressure still higher. The bradycardia and hypertension seem to be independent phenomena which are closely associated by reason of being induced frequently by the same stimulus.

In man we have artificially elevated the intracranial pressure nearly as high as the mean blood pressure (which is usually about 1,300 mm. of saline) and have not induced the Cushing phenomenon. In special circumstances we have elevated the intracranial pressure to 2,000 mm. of saline without the subject's awareness of any sensation. Occasionally, hypertension, tachycardia and tachypnea appeared gradually an hour or so after the procedure was started, usually beginning when the intracranial pressure had been considerably elevated (800 to 1,000 mm. of saline) and subsiding over a period of about an hour (figs. 8 to 12). Restlessness, confusion and evidence of anxiety were usually associated. The particular cause for this reaction has not been determined as yet; it may well not be due either to the artificial elevation of the intracranial pressure or to the addition of saline solution to the subarachnoid space.

SUMMARY

In most of the patients whom we have studied the intracranial pressure can be elevated rather abruptly to 1,000 mm. of saline solution without the slightest immediate effect on the pulse, respiration or blood pressure or without the subject's awareness of any sensation. This rise is much higher than the usual spontaneous rise in the intracranial pressure in fatal cases of acute intracranial hemorrhage or neoplasm. Sometimes the procedure is followed by transient hypertension, tachycardia and tachypnea.

We have repeatedly induced in monkeys the hypertension, bradycardia and apnea described by Cushing in dogs in circumstances in which the intracranial pressure approaches the arterial pressure. As Cushing noted, the reflex reactions do not depend on the height of the intracranial pressure but more directly on its relation to the arterial pressure. This triad of reflex responses was not observed together in the human subjects whom we studied with initial normal or elevated intracranial pressures, even though many had intracranial pressures as high as those usually found with intracranial neoplasms and even though in most of them the intracranial pressure was artificially elevated considerably above this level, although still below the arterial pressure.

These observations are in accord with clinical experience that the doctrine which holds that "an increase in intracranial tension occasions a rise in blood pressure, which tends to find a level slightly above the pressure exerted against the medulla" [1] is not often useful in the diagnosis and management of disorders associated with high intracranial pressure. The usual mechanism by which the cerebral blood flow is adjusted for the decrease in the pressure head of blood flowing into the brain occasioned by elevation of the intracranial pressure appears to be immediate reflex dilatation of the cerebral arterioles rather than an increase in blood pressure. This primary adjustment is not associated with any other vascular or respiratory reflex response.

Signs and symptoms other than the Cushing phenomenon must be depended on for the proper handling of the emergency patient with high intracranial pressure.

NONMALIGNANT INTRINSIC STRICTURE OF THE PANCREATIC DUCT

Report of a Case

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THERE would appear to be little in the literature concerning intrinsic strictures of pancreatic ducts and most of the references have to do with malignant growths or with stones. While many ducts are undoubtedly acutely blocked because of edema in associated acute pancreatitis, this condition is usually temporary and clears without any strictural sequelae referable to the ducts. The following case of an apparently idiopathic benign stricture of the pancreatic duct within the substance of the head of the pancreas causing chronic retention and distention of the pancreatic duct radicals, cured by simple dilatation and intubation of the duct in an unusual way, would appear to be unique.

W. J. B. aged 59, single, a first aid man, consulted Dr. J. W. Caldwell on June 11, 1949. The complaint was diarrhea of two to three months' duration occurring every second year since 1939, diffuse pain in the upper part of the abdomen, cramps at stool and a recent weight loss of 10 pounds (4.5 Kg.). The history revealed no illnesses of consequence and no operations. The patient had considerable nocturia but was not seriously troubled by anything other than the intermittent diarrhea and recent pain. The history revealed no relevant diseases.

Examination revealed a tall thin man of the cadaverous type; the color was good, and there were no obvious physical defects. The weight was 125 pounds (56 Kg.), the blood pressure 110/70 and the pulse rate 60. There was tenderness over the epigastrium, and moderate scoliosis was present. The prostate was large and smooth.

Laboratory Investigation.—The red blood cell count was 4,780,000, white blood cell count 13,500; hemoglobin 92 per cent (14.35); sedimentation rate 12 mm., and color index, 0.97. The Kahn reaction was negative. The icterus index was 6 units; the cephalin flocculation test gave a negative reaction. The blood amylase level was 33 units. Fractional gastric analysis showed the presence of achlorhydria, and the total acid range was between 15 and 27. The patient was unresponsive to histamine. No blood or bile was present. Urinalysis showed a specific gravity of 1030, no sugar or albumin and an acid reaction.

Course in the Hospital.—On Aug. 8, 1949, the patient was seen again, complaining of loose stools and bandlike pain over the upper area of the abdomen. A series of roentgenograms on August 12 revealed a normally functioning gallbladder, negative for opaque calculi. A preliminary roentgenogram of the gastrointestinal tract showed "moderate scoliosis with convexity to the left. There are some radiopaque densities over the right sacroiliac region, possibly calcified glands. The aorta shows some calcification. Screening of the chest gives negative results. Barium is swallowed without difficulty. The stomach is somewhat ragged and hypermotile but empties readily, and there is no evidence of a lesion. The duodenal cap is large and dilated, and there is a persistent filling defect in the distal portion of the cap. This may be either intrinsic or extrinsic. A six hour roentgenogram shows no gastric residue. In the colon, barium passed without obstruction. The transverse colon is ptotic and lies well down within the pelvis. The postevacuation roent-

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genogram shows no evidence of an infiltrative lesion. Filling of the appendix is noted. The conclusion is that a large filling defect is present in the distal portion of the duodenal cap, possibly an extrinsic or intrinsic lesion. Essentially negative results were obtained after a barium enema."

On August 16 the patient was seen by me in consultation and the above findings were confirmed. The diagnosis was probable neoplastic disease of the head of the pancreas or the second portion of the duodenum.

On Sept. 1, 1949, exploratory laparotomy was performed. "The abdomen was opened with an upper right rectus incision. The duodenum was found to be edematous; the pancreas was hard and tense and looked as though the pancreatic duct must be obstructed, with retention in the ducts. The duodenum was mobilized, and the common duct was examined and was definitely not dilated. The gallbladder appeared normal and emptied readily on pressure. The liver was normal; material for a biopsy was taken. The rest of the abdomen was normal except for a tiny hard nodule on the left side of the crus of the left diaphragm. The pelvis was normal; there was just a suggestion of fluid in the bottom of it. The small bowel contained numerous diverticula of the congenital type. The duodenum was opened and the ampulla explored and found to be normal.

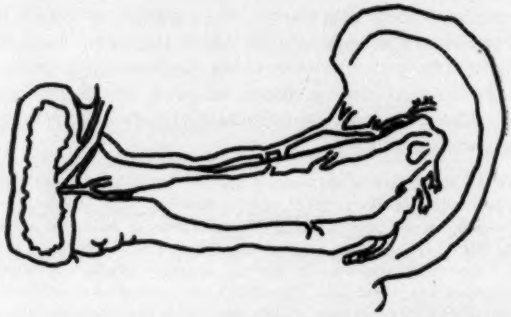

Fig. 1.—The darkened area represents the region of strictured duct and large lakelike ducts behind the stricture.

The pancreas contained a hard nodule in the head and several others scattered through it. One of these was excised and was given to the pathologist, Dr. Pitts, who proclaimed it to be nonmalignant.

In consequence, the neck of the pancreas was transected, and there was a great rush of pent-up pancreatic fluid, with about 4 ounces (120 cc.) escaping. Probes would enter the bile duct with ease through the ampulla but would go only 3/8 inch into the pancreatic duct. There was a definite stricture in the pancreatic duct just inside the head. This was dilated up from the pancreatic end of the transected duct to an 8 mm. size by DeBakes dilators and a rubber tube passed through the ampulla of Vater, through the duct and into the ducts in the tail of the pancreas. The neck of the pancreas was reanastomosed over the indwelling rubber tube, which was anchored in the duodenum with plain surgical gut. The tip projected through the ampulla into the third part of the duodenum. The duodenum was then closed, and the gallbladder itself was anastomosed to the jejunum, which was brought up over the transverse colon and anchored there to the falciform ligament and the anterior surface of the stomach to obviate ampullary obstruction from the indwelling tube. The abdomen was closed without drainage after the use of penicillin and sulfonamide crystals."

"This is definitely a case of inflammatory stricture of the pancreatic duct which has been treated by dilatation and dowel tube type of reconstruction. It is not believed to be malignant. The immediate postoperative condition is good."

Pathological Report.—A. Specimen of Nodes from Pancreas: Gross Observations.—The specimen is a pea-sized piece of fairly firm, grayish pink tissue. Two other small lymph nodes,

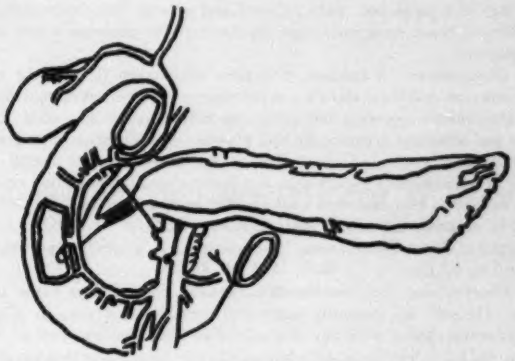

Fig. 2.—Site of transection of ducts and method of exploration.

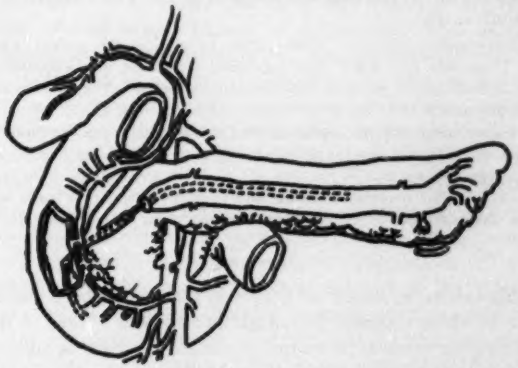

Fig. 3.—Restoration of ducts over indwelling tube.

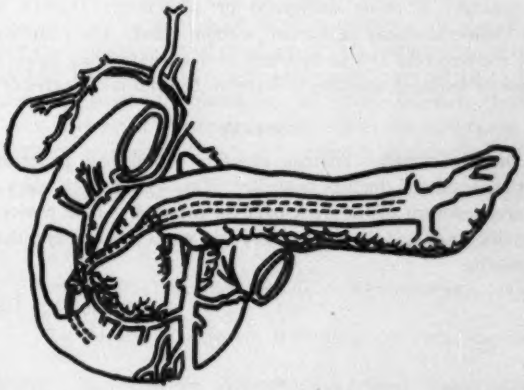

Fig. 4.—Completed operation, with dowel arrangement of indwelling tube.

each about the size of a large pea, were received and a large lima bean-sized piece of rather firm, rubbery, fibrotic tissue apparently from the head of the pancreas which grossly does not appear to be malignant.

Microscopic Observations. A number of sections were taken through the small portion of tissue from the pancreas, and these show a marked degree of rather edematous fibrosis surrounding islands of compressed-appearing but otherwise normal pancreatic acini, ducts and islets. There is diffuse and abundant lymphocytic and plasma cell infiltration throughout but no suggestion of a malignant process. Section through the small separate lymph nodes shows a moderate degree of inflammatory hyperplasia, and another small firm section received separately shows a picture similar to that described above in the pancreatic tissue.

Diagnosis. The diagnosis is chronic pancreatitis.

B. Liver Biopsy: Gross Observations. The specimen is a corelike portion of liver tissue measuring about 2 by 0.2 cm.

Microscopic Observations. Sections through the small core of liver tissue show no definite sclerotic process. The cells are generally fairly well preserved and show an abundant glycogen content. There does not appear to be any evidence of an inflammatory process.

Postoperative Course.—The postoperative course was uneventful. Three months later the diarrhea had stopped, and the patient had gained 10 pounds (4.5 Kg.) in weight; he had no further steady pain but had occasional attacks of cramping pain in the abdomen. A roentgenogram showed the tube still in situ.

Follow-Up Observations, October, 1950.—After 13 months the patient was well, with a weight gain of 17 pounds (7.7 Kg.). The red blood cell count was 4,660,000, the white cell count 2,550, the hemoglobin 91 per cent and the color index 0.99. The differential count was as follows: polymorphonuclear cells, 66; lymphocytes, 27; monocytes, 4, and eosinophils, 3. A blood smear showed the red blood cells to appear normal in size, shape and hemoglobin content. The platelets were normal. The van den Bergh indirect reaction showed less than 0.5 mg. of bilirubin per 100 cc. The serum amylase was 73 mg. per 100 cc. (Somogyi method, 40 to 110 mg.), and the urine amylase was 10 units (normal 8, to 32 units). A roentgenogram made in October 1950, showed that the tube had passed out unrecognized since the last investigation eight months previously.

COMMENT

I believe this case to be somewhat unique in that I have been unable to discover any other case in which a similar pathologic process was treated in this way. The literature touching on intrinsic strictures of pancreatic ducts is sufficiently meager to warrant bringing this case to the attention of surgeons. There must be many such patients in whom the abdomen is explored and closed on the assumption that the swollen pancreas is either malignant or subacutely inflamed and a choledochotomy or cholecystostomy performed without relief. The complete transection of the neck of the pancreas and its resuture over an indwelling dowel type of tube, without leakage or sequelae, are also believed to be unusual features of this case.

SUMMARY

A case of benign idiopathic intrinsic stricture of the main pancreatic duct with pent-up secretion in dilated ducts is described. Transection of the neck, dilatation of the stricture and resuture of the neck over an indwelling tube projecting into the duodenum are discussed and depicted. Recovery was complete, and the tube passed out in eight months.

INTERNAL DRAINAGE OF PANCREATIC CYST BY MEANS OF A ROUX-Y ANASTOMOSIS TO THE JEJUNUM

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CHICAGO

COMPLETE resection of a pancreatic cyst, although the procedure of choice, is often technically difficult or impossible to perform, so that an alternative operation such as external or internal drainage of the cyst becomes necessary. Drainage operations, whether of the internal or external type, are contraindicated in the treatment of multilocular tumors of the pancreas such as cystadenomas, cystadenocarcinomas or dysontogenetic cysts. Complete resection of these tumors offers the only possibility of a cure. Unilocular cysts such as the retention and pseudocysts of the pancreas are suitable for internal or external drainage.

External drainage, or so-called marsupialization, of pancreatic cysts, which was first carried out by Gussenbauer [1] in 1882, remains today the most frequently performed operation for these cysts. Internal drainage may be accomplished either by inserting multiple drains into the cyst cavity or by suturing the edge of the opening in the cyst wall to the cut edge of the parietal peritoneum surrounding the incision on the anterior abdominal wall. These cysts may also be drained through a left posterior lateral incision that reaches the cyst anterior to the kidney. External drainage is followed by prolonged draining wounds, often secondary infection of the cyst and not infrequently digestion of the skin by the pancreatic enzymes. Persistent fistulas of the abdominal wall may follow external drainage of true cysts of the pancreas. This complication often requires resection of the fistula and the pancreas or drainage of the fistula into the upper intestinal tract.

In order to prevent the prolonged draining wounds, persistent fistulas and secondary sepsis that follow external drainage of pancreatic cysts, internal drainage was first advised by Jedlicka.[2] He resected the major part of the cyst and anastomosed the remaining part to the posterior wall of the stomach. Jurasz,[3] without resecting the cyst, performed an anastomosis between the pancreatic cyst and the posterior wall of the stomach. Kerschner [4] united a pancreatic cyst to the duo-

Read at the Fifty-Eighth Annual Meeting of the Western Surgical Association, Minneapolis, Dec. 2, 1950.

1. Gussenbauer, C.: Zur Casuistik der Pankreascysten, Prager Med. Wchnschr. **19**:15, 29, 1894.

2. Jedlicka, R.: Eine neue Operationsmethode der Pancreascysten (Pancreatogastrostomie), Zentralbl. Chir. **50**:132, 1923.

3. Jurasz, A.: Zur Frage der operativen Behandlung der Pankreascysten, Arch. klin. Chir. **164**:272-279, 1931.

4. Kerschner, F.: Transduodinale Anastomosierung einer Pancreascysten mit dem Duodenum, Beitr. klin. Chir. **147**:28-33, 1929.

denum, and Hahn [5] anastomosed these cysts to the jejunum. Hamesfahr,[6] Walzel [7] and Neuffer [8] were the first to advise draining pancreatic fistulas and cysts into the gallbladder. Since the early reports of these authors internal drainage of pancreatic cysts has been done with increasing frequency. There has been a surprisingly low incidence of septic complications as a result of the intestinal contents entering the pancreatic cyst. Of the various anastomoses between the pancreatic cyst and the upper intestinal tract, the anastomosis between the cyst and the jejunum offers the greatest adaptability. An improvement of the original operation advised by Hahn which allowed the free passage of jejunal contents into the cyst is an operation advised by Greisman,[9] Migliaccio and Laurelli [10] consisting in a Roux-Y anastomosis between the jejunum and the pancreatic cyst. The Roux-Y anastomosis prevents the regurgitation of the intestinal contents into the cyst and overcomes many of the theoretical objections to performing an internal drainage operation as a primary procedure in the treatment of pancreatic cysts.

REPORT OF CASES

Case 1.—Mr. J. W., aged 45, was admitted to the Cook County Hospital in Nov. 11, 1947. Three months before his admission, while driving an automobile, he was in an accident during which he was thrown forward against the steering wheel in such a way as to strike the steering wheel with the upper part of his abdomen. He was hospitalized elsewhere for emergency treatment. About 10 days after the injury he entered the Cook County Hospital. Physical examination on his admission showed his abdomen to be distended with what appeared to be fluid. This diffuse distention gradually subsided, and a slightly tender mass could be palpated in the upper region of the abdomen. The patient began to experience severe burning epigastric pain associated with nausea.

Roentgen examination of the upper part of the intestinal tract showed a large mass (fig. 1). The mass displaced the stomach anteriorly and upward. The duodenal curve was wide. A roentgen diagnosis was made of a probable pancreatic cyst.

On Nov. 24, 1947, with the patient under cyclopropane-oxygen anesthesia, the abdomen was explored. The lesser peritoneal cavity, which was explored through an opening in the gastrocolic omentum, was filled with a cystic mass, from which there was aspirated about 1,500 cc. of straw-colored fluid. The fluid on subsequent examination was shown to contain pancreatic enzymes. The cyst was marsupialized by suturing the cyst wall surrounding the opening to the cut edge of the adjacent parietal peritoneum and the skin of the abdominal incision.

The immediate postoperative course was uneventful. The patient was discharged on Dec. 24, 1947, at which time the sinus into the cyst was still draining. About three months postoperatively the abdominal sinus closed, after which time he began to experience recurrence of the severe burning epigastric pain.

A mass again gradually developed in the epigastrium and his pain increased in severity. The old sinus tract was reopened and the same type of straw-colored fluid obtained at the original operation escaped from the cyst. The patient got immediate relief of pain. During

5. Hahn, O.: Zentralbl. Chir., Nov. 6, 1932; cited by Neuffer, H.: Arch. klin. Chir. **170**: 488-492, 1932.

6. Hamesfahr, cited by Walzel, P.: Mitt. Grenzgeb. Med. u. Chir. **40**:71-182, 1927.

7. Walzel, P.: Innere Drainage einer Pancreascysten unter Ausnutzung des Resorptionsvermögens der Gallenblase, Mitt. Grenzgeb. Med. u. Chir. **40**:71-182, 1927.

8. Neuffer, H.: Zur operativen Behandlung der Pancreascysten, Arch. klin. Chir. **170**: 488-492, 1932.

9. Greisman, H.: Zur Behandlung der Pankreascysten, Chirurg. **19**:302-306, 1948.

10. Migliaccio, A. V., and Laurelli, E. C.: Pancreatic Cyst: Internal Drainage Utilizing the Roux Principle, Surgery **24**:54-56 1948.

the ensuing 12 months the sinus closed on three occasions, with recurrence of pain and subsequent relief of pain on reopening of the sinus tract. His distress was severe and persistent enough to prevent his retaining any gainful employment.

He was readmitted to the Cook County Hospital on Jan. 7, 1949, for the purpose of reoperation. On Jan. 16, 1949, with the use of cyclopropane-oxygen anesthesia, the abdomen was reopened. The pancreatic cyst had decreased to about one-half its original size. The site of the old sinus tract which presented itself through the gastrocolic omentum was enlarged to about 2 cm. in diameter. A Roux-Y type of anastomosis was performed between the cyst and the jejunum (fig. 2). The loop of jejunum between the cyst and the enteroanastomosis was about 30 cm. long and was brought anterior to the transverse colon. The anastomosis between the end of the jejunum and the opening in the pancreatic cyst was performed by means of two layers of black silk (0000). The enteroanastomosis was performed with a row of continuous

Fig. 1.—Roentgen examination in case 1 shows tumor in region of head of pancreas. The tumor displaces the stomach upward, and there is a widening of the duodenal loop.

surgical gut (0000) mucosal sutures and a second layer of interrupted silk (0000) seromuscular sutures. The abdominal wall was closed with interrupted wire sutures and without drainage. The postoperative course was uneventful.

Since his second operation, 25 months ago at the time of this report, the patient has been free of pain, has gained 25 pounds (11.3 Kg.) in weight and has been working steadily as a day laborer.

Roentgen examination of the upper gastrointestinal tract taken 22 months postoperatively showed no barium sulfate entering the cyst (fig. 3).

Case 2.—Mr. R. B., aged 35, was admitted to the Cook County Hospital on Jan. 3, 1950. In 1940 he noted the gradual onset of recurring episodes of upper abdominal pain. The pain was usually sudden in onset, sharp and often intense. It would occur in either the right or the left upper quadrant and frequently radiated straight through to the left lower dorsal area. It would last from several minutes to days, would often be severe enough to require narcotics for relief and was often accompanied with nausea and anorexia. The patient had lost about 35 pounds (16 Kg.) in weight in a two year period. During this two year period he experienced a gradually increasing diarrhea. His stools contained fat particles which seeped through the anus and soiled his underclothing.

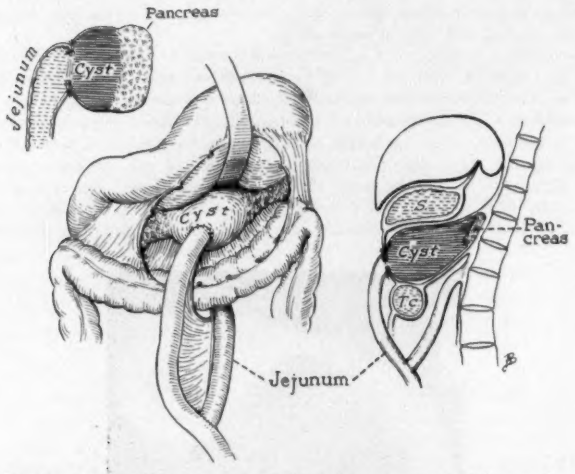

Fig. 2.—Pseudocyst of the pancreas is drained into the upper jejunum by means of a Roux-Y anastomosis. The loop of jejunum draining the cyst is brought anterior to the transverse colon.

Fig. 3.—Roentgen examination in case 1 performed 22 months after Roux-Y pancreatic cyst-jejunum anastomosis failed to show any barium entering the cyst.

In December 1948 the patient was admitted to a hospital elsewhere. Review of the hospital record showed that a diagnosis was made of chronic fibrosing pancreatitis, with diffuse calcification and pancreatic calculi. A right splanchnic sympathectomy was done, but he obtained little or no relief. During a period of hospitalization elsewhere a mass was palpated in the right upper quadrant. The mass was said to have changed in size. The remaining history was noncontributory in reference to his present problem.

Physical examination on his admission to the hospital showed a 7 cm. mass in the right upper quadrant directly adjoining the midline of the abdomen. The mass was smooth, round and tender. Except for a lumbar scar and malnutrition, there were no other abnormalities. The laboratory examination showed a red blood cell count of 3,710,000 with hemoglobin

Fig. 4.—Roentgen examination in case 2 shows a tumor in the head of the pancreas. The duodenal loop is widened. There are scattered areas of calcification throughout the head and body of the pancreas.

87 per cent, and a white blood cell count of 9,999. A dextrose tolerance test showed a normal curve. The Kahn reaction was negative, and the blood amylase level was 16 units. Cholecystography showed a normal gallbladder and no stones.

A roentgenogram was made of the stomach and showed it to be normal. The duodenal loop was wide and the duodenum was narrowed as a result of a mass that seemed to be in the head of the pancreas (fig. 4). There were many small calcifications in the region of the head and body of the pancreas. Roentgen studies of the colon showed no pathologic changes.

While the patient was in the ward under observation he required frequent injections of morphine sulfate, ¼ grain (15 mg.), for relief of the abdominal pain.

On January 16, with the patient under nitrous oxide-oxygen-ether anesthesia, the abdomen was opened. The pancreas was thickened, firm and infiltrated throughout with small areas of

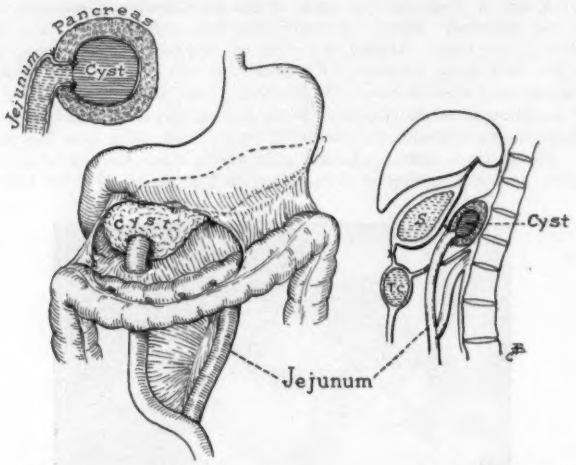

Fig. 5.—A retention type cyst in the head of the pancreas is drained into the jejunum by means of a Roux-Y anastomosis. The loop of jejunum draining the cyst is brought through an opening in the transverse mesocolon.

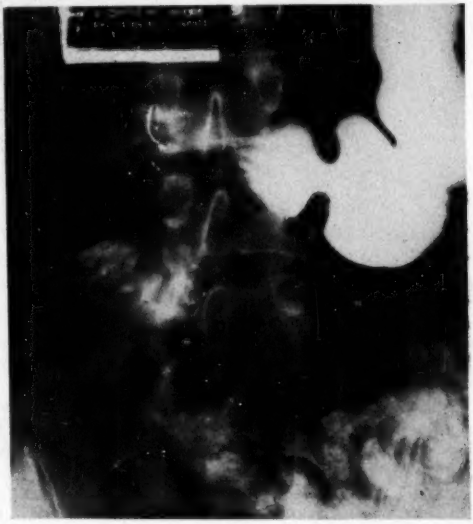

Fig. 6.—Roentgen examination in case 2 performed 10 months after a Roux-Y pancreatic cyst-jejunum anastomosis failed to show any barium entering the cyst.

calcification. Deep in the head of the pancreas there was a cyst that measured about 6 cm. in diameter and from which a thin whitish fluid was aspirated. The remaining abdominal viscera were grossly normal.

An operative diagnosis was made of a chronic fibrosing pancreatitis with calcification, possible calculi, and a cyst, probably a retention type cyst, in the head of the pancreas. A Roux-Y type of anastomosis was done between the cyst of the pancreas and the jejunum (fig. 5). The loop between the cyst and enteroanastomosis was made about 30 cm. long and was brought posterior to the transverse colon, through an opening in the transverse mesocolon. The anastomosis between the cyst and jejunum was made with two layers of interrupted (0000) black silk. The enteroanastomosis was performed in two layers, a mucosal layer of continuous (0000) surgical gut and a second seromuscular layer of interrupted (0000) black silk. The abdominal wall was closed with interrupted wire sutures and without drainage.

The postoperative course was uneventful. The patient obtained immediate relief of his pain. He has gained about 40 pounds (18 Kg.) in weight. His diarrhea has subsided, with the aid of small doses of pancreatic extract, and his stools are more normal in appearance. Roentgen studies of his upper gastrointestinal tract done in November 1950 showed a normal stomach and a normal duodenal curve, and no barium sulfate could be forced into the cyst (fig. 6). When last seen in February 1951, he continued to be free of distress. He was working at his previous employment and no longer required any medication except the pancreatic extract.

COMMENT

Although pancreatic cysts have been drained into all portions of the upper intestinal tract, drainage into the jejunum by means of a Roux-Y anastomosis seems to offer a greater adaptability and is a more physiologic operation in so far as it drains the pancreatic juice into the intestine, where it normally enters, rather than into the stomach or gallbladder. The free loop of jejunum draining the cyst may be brought anterior to the colon and anastomosed to the cyst through an opening in the gastrocolic or gastrohepatic omentum.

This anterior type of anastomosis, since it requires only a limited dissection of the pancreatic cyst, seems more suitable for drainage of pseudocysts or of pancreatic fistulas which are surrounded by often severe subacute and chronic inflammatory reaction. The free loop of jejunum may be brought through an opening in the transverse mesocolon and to the pancreatic cyst. This posterior type of anastomosis is especially suitable to the drainage of cysts situated in the head of the pancreas, as in case 2. From a functional standpoint, either type of jejunal anastomosis, whether placed anterior or posterior to the transverse colon, gives equally good results.

In the Roux-Y type of anastomosis the peristalsis in the free loop of jejunum anastomosed to the cyst is away from the cyst and toward the jejunojejunal anastomosis. This downward peristaltic gradient in the jejunal loop prevents the intestinal contents from entering the cyst and reduces the incidence of septic complications which have been reported to have occurred [11] after jejunopancreatic cyst anastomoses.

By so preventing the intestinal contents from entering the cyst and reducing the possibility of infection, the theoretical objection to draining pancreatic cysts or fistulas into the jejunum is overcome. Drainage of true pancreatic cysts into the jejunum prevents the loss of the external pancreatic secretion and alleviates the symptoms of pancreatic deficiency, as occurred in one of our cases (J. B.).

11. Meyer, K. A.; Sheridan, A. I., and Murphy, R. F.: Pseudocysts of the Pancreas, Surg., Gynec. & Obst. **88**:219-229, 1949.

The continued patency of an anastomosis between the jejunum and pancreatic cyst may be questioned. As far as we were able to find, there have been no reported cases in which stenosis or obliteration of the cyst-jejunum anastomosis has caused a recurrence of the symptoms or signs of a pancreatic cyst.

SUMMARY

Roux-Y anastomosis between a pancreatic cyst and the jejunum in the two cases herein reported relieved the symptoms of a pancreatic cyst. The indication for this type of anastomosis is limited to nonresectable solitary cysts of the pancreas, pseudocysts, and the benign cysts of the head of the pancreas when internal drainage seems more advisable than a pancreatic resection. The anastomosis prevents the intestinal contents from entering the cyst and reduces the incidence of infection of the cyst or the adjoining pancreas.

In the two cases presented in this report it was impossible during fluoroscopic examination of the upper intestine to force barium sulfate from the jejunum into the cyst.

Internal drainage of cysts that contain pancreatic secretions may alleviate symptoms that result from a loss or deficiency of the external pancreatic secretion.

Internal drainage of pancreatic cysts into the jejunum by means of a Roux-Y anastomosis is suggested as a primary procedure in the treatment of the solitary benign cysts or pseudocysts of the pancreas.

DISCUSSION

Dr. Stanley R. Maxeiner, Minneapolis: I have had no experience with the Roux-Y type of operation for this procedure, but we did have a trying experience in which we anastomosed the cyst to the posterior wall of the stomach. This case was written up a year or so ago by my son and myself and was published in *Surgery* **27**:919-921 (June) 1950.

The patient was first seen by us during an acute attack of pancreatitis. A mass subsequently developed in his abdomen which evidently represented the pancreatic cyst. We operated on him and found that the cyst was adherent to the posterior wall of the stomach. It was such a simple procedure to make an incision in the wall of the stomach and into the cyst and complete the anastomosis that we proceeded to do so.

On the sixth postoperative day a massive hemorrhage developed. The patient went into shock and collapsed, and the blood pressure could not be obtained. We went through that experience again, and we did not dare to postpone operation, so we operated on him a second time.

The cyst had apparently disappeared, but he had an active ulcer at the site of the anastomosis. We excised the ulcer, restored the posterior wall of the stomach, and did nothing further because the patient's condition was so critical. One week later another hemorrhage developed. He went through six of these episodes, the last one warning us that we could not let him go any longer.

Contemplating another hemorrhage (they came at about six day intervals usually), we took him to the operating room during the night. We had three portals of entry for blood. The man started to bleed and we gave him 22 units of blood (11,000 cc.) on the table. I never came so close to losing a patient on the table as on that occasion.

We did a gastric resection and a posterior anastomosis. The patient is well today. It was a desperate experience. I would not thoroughly endorse the posterior anastomosis to the stomach, but the Roux-Y operation may not be followed by such complications.

Dr. L. B. Johnston, Cincinnati: I wish to mention two cases of internal drainage of pancreatic cyst in which I used a jejunal loop with enteroanastomosis at the base of the loop. The first case was that of a 3 year old boy who presented a picture of an acute abdominal con-

dition. He had a huge upper right abdominal mass which proved to be a markedly distended retroperitoneal cyst. It contained slightly bile-tinged fluid which on subsequent examination showed the presence of pancreatic enzymes.

At the operation the cyst was marsupialized and drained, the drains having been brought out far to the right. The copious drainage of fluid from day to day did not diminish, and at the end of a week we had difficulty in maintaining the child's fluid and electrolyte balance.

At that point I asked Dr. Max Zinninger to see him with me, and it was agreed that an internal drainage would have to be done. It did not seem feasible to use the duodenum, which was lying directly over the hard cyst, for fear that the duodenal content would go directly into the cyst. Therefore, we used a jejunal loop with enteroanastomosis at the base of the loop. The child recovered uneventfully. At the end of the three months there was a moderate amount of air in the partially collapsed cyst cavity, and at the end of a year there was a slight amount of air. It has been three years since then, and the child has remained well, without any recurrence of the cyst.

The other case that I wish to mention was that of a 37 year old man who in the course of two years had two pancreatic cysts. The one to the left was satisfactorily obliterated by two drainage procedures. The one which was closer to the midline, when it became tense and enlarged, caused jaundice. It recurred after one drainage procedure, and a few months ago we treated it by internal drainage. So far the patient has had no recurrence.

I might add that in using the same type of jejunal loop for the purpose of cholecystojejunostomy in a small number of cases of pancreatic carcinoma I have seen no instance of subsequent biliary tract infection. The procedure which I have done may be a little easier and quicker to perform than the Roux-Y procedure, but from an anatomical and physiological standpoint it would seem to me that the procedure which Dr. Rosi has done is probably preferable.

SYMPATHETIC NERVE BLOCK IN EARLY ACUTE CHOLECYSTITIS

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AND
NATHAN A. WOMACK, M.D.
IOWA CITY

THE MAJORITY of the nerve fibers that are distributed to the biliary tree are derived from the sympathetic system and reach the liver by way of the celiac plexus. Those vagal fibers involved come chiefly from the right vagus and pass to the celiac ganglions, where they become incorporated in some of the sympathetic trunks.

The sympathetic fibers are derived from the greater splanchnic nerves having their origin predominantly from the sixth to the ninth thoracic sympathetic ganglions and occasionally from the lesser splanchnic nerves which arise from the tenth to the twelfth sympathetic ganglions.[1]

Our experience confirms the findings of Raigorodsky,[2] who divided the hepatic plexus, which is formed by the fibers approaching the liver from the celiac plexus, into anterior and posterior portions. The anterior hepatic plexus always follows the hepatic artery, the pathway changing as the course of the artery varies. The posterior hepatic plexus of nerves passes to the right superiorly in the portal area, where at first it lies behind the lower third of the portal vein and crosses over on the undersurface; it is then found lying in the outer groove between the right periphery of the portal vein and the common bile duct. From here it passes to the liver, which it enters in the region of the end branches of the right hepatic artery. Along the course of the right hepatic artery it anastomoses with ramifications of the anterior hepatic plexus.

As both plexuses approach the region of the common bile duct several large nerves that supply the common bile duct and the gallbladder emerge. The medial nerve of the gallbladder arises from the anterior plexus, passes over the surface of the common and hepatic ducts, anastomoses with the posterior hepatic plexus in the triangle of the cystic and hepatic ducts and passes to the medial surface of the gallbladder.

The lateral nerve of the gallbladder arises from the posterior plexus and passes along the lateral surface of the common and cystic bile ducts to the lateral and inferior surfaces of the gallbladder.

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1. Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea and Febiger, 1934.

2. Raigorodsky, J. L.: Die Nerven der Leberpforte des Menschen, Ztschr. Anat. u. Entwg. **86**:698-730, 1928.

The pancreaticocholedochus nerve as described by Latarget [3] is derived from the posterior plexus and passes distally to the retroduodenal and intraduodenal portions of the common bile duct.

The common bile duct is therefore surrounded by a delicate net of nerve fibers throughout most of its extent. These fibers are much more numerous in the region of the junction of the cystic and common hepatic ducts, where they form the main trunks supplying the gallbladder and the extrahepatic ducts.

In the muscularis of the gallbladder one often encounters single ganglion cells or small clusters of them that probably represent vagal pathways. Sympathetic fibers may stop in the musculature or extend through and apparently terminate in the mucosa or possibly between the epithelial cells of the mucosa. These fibers have no specialized end organs but terminate as exposed raw nerve fibers.

That this nerve supply to the gallbladder and the extrahepatic duct system may be considerably involved in inflammatory lesions of the gallbladder has been previously demonstrated.[4] These inflammatory changes consist chiefly of fibrosis, edema and exudation and result in relative ischemia and stretching of the nerve fibers and trunks. There is also the additional action of the stimulating effects of inflammatory metabolites such as lactic acid and the release of potassium ions as well as pH changes. The resultant effect varies from one of intense stimulation of this nerve supply in the acute phase to a lowered threshold of stimulation with periodic exacerbations in the so-called chronic stages. That such stimulation will reproduce the pain and dyspepsia so characteristic of cholecystitis has been amply demonstrated.[5]

As an adjuvant in the treatment of acute cholecystitis a simple method of relieving pain and aiding in the subsidence of smooth muscle spasm would be of great benefit. That such would take place if the right sympathetic trunk were anesthetized by means of the injection of procaine seemed probable.

As early as 1923 Lawen [6] used paravertebral injection of procaine for the relief of pain from abdominal viscera in cases of malignant disease and other types of chronic painful conditions of the biliary system. He made use of it as well for the differential diagnosis of organs affected. His studies, aided by those of others,[7] have made it possible to map out segments which transmit sensation from the gastrointestinal tract. Davis, Pollock and Stone showed that gallbladder pain is

3. Latarget, P. B., and Bonniot, A.: Les nerfs du foie et des voies biliares, Lyon Chir. **17**:1-39, 1920.

4. Womack, N. A.: Pathologic Changes in Chronic Cholecystitis and the Production of Symptoms, Surgery **4**:847-855, 1938. Womack, N. A., and Crider, R. L.: The Persistence of Symptoms Following Cholecystectomy, Ann. Surg. **126**:31-55, 1947.

5. Schrager, V. L., and Ivy, A. C.: Symptoms Produced by Distention of the Gallbladder and Biliary Ducts, Surg., Gynec. & Obst. **47**:1-13, 1928. Davis, L.; Hart, J. T., and Crain, R. C.: The Pathway for Visceral Impulses Within the Spinal Cord, ibid. **48**:647-651, 1929. Butsch, W. L.; McGowan, J. M., and Walters, W.: Clinical Studies on the Influence of Certain Drugs in Relation to Biliary Pain and to the Variations in Intrabiliary Pressure, ibid. **63**:451-456, 1936. Doubilet, H., and Colp, R.: Resistance of the Sphincter of Oddi in the Human, ibid. **64**:622-623, 1937.

6. Lawen, A.: Weitere Erfahrungen über paravertebrale Schmerzaufhibung zur Differentialdiagnose von Erkrankungen der Gallenblase, des Magens, der Niere und des Wurmfortsatzes sowie zur Behandlung postoperative Lungenkomplikationem, Zentralbl. Chir. **50**:461-465, 1923.

7. Alvarez, W. C.: Abdominal Pain: Paths Over Which It Travels and Ways in Which These May Be Blocked, Am. J. Surg. **14**:385-394, 1931.

referred chiefly over the right major splanchnic nerve in animals,[8] and Craig treated chronic biliary tract pains by means of splanchnicectomy.[9] Mandl [10] has used paravertebral block with procaine and in some cases with alcohol in the treatment of the pain of chronic cholecystitis.

TECHNIQUE

The method of paravertebral block that we have used is similar to that recommended by Labat.[11] Skin wheals are raised 4 cm. to the right of the upper third of the eighth and ninth spinous processes. A 10 cm. needle is introduced through the wheal perpendicular to the skin until rib or transverse process is contacted. The needle is then withdrawn to the subcutaneous tissue and advanced in a slightly medial and caudal direction until the body of the vertebra is touched. The needle is then withdrawn and reinserted more laterally until it will advance along the lateral portion of the body of the vertebra 1 cm. farther than the depth at which the vertebral body was contacted. Small amounts of procaine are injected as the needle is being advanced to

Results of Procaine Block in Patients with Acute Cholecystitis

Patient	Proposed Diagnosis	Result of Block	Pathological Diagnosis
K. S.	Acute cholecystitis	Relief of symptoms; subsidence of jaundice	Acute cholecystitis subsiding
O. W.	Acute cholecystitis	Relief of symptoms	Edema of gallbladder; acute cholecystitis subsiding
M. D.	Acute cholecystitis	Relief of symptoms	Acute cholecystitis subsiding
E. G.	Acute cholecystitis	Relief of symptoms	Acute cholecystitis subsiding
R. H.	Acute cholecystitis	Relief of symptoms	Acute cholecystitis subsiding
M. S.	Acute cholecystitis	Relief of symptoms	Acute cholecystitis subsiding
O. C.	Acute cholecystitis	Relief of symptoms	Acute cholecystitis subsiding
M. W.	Psychoneurosis; right upper quadrant pain	No change in symptoms	Operation not indicated
A. R.	Psychoneurosis; right upper quadrant pain	No change in symptoms	Operation not indicated
I. G.	Typhoid; cholangitis, severe	No change in symptoms	Cholangitis, liver abscesses, adhesions to parietal peritoneum
F. R.	Ruptured gallbladder	No change in symptoms	Ruptured gallbladder with subphrenic abscess
J. B.	Postcholecystectomy symptoms	Relief of symptoms precipitated by cream and butter	Long dilated cystic duct stump with scar tissue enmeshing sympathetic nerves
M. P.	Acute cholecystitis	Relief of pain; subsidence of jaundice	Normal gallbladder; liver biopsy—cholangitis and congestion
J. Mc.	Pyloric ulcer with gastric retention	Relief of symptoms	Normal gallbladder; vagotomy and gastrojejunostomy performed

reduce the discomfort of the procedure. When the needle has been accurately placed, 5 to 10 cc. of 2 per cent procaine is injected. Care must be taken to stay close to the vertebral body to prevent entering the pleura and lung since pneumothorax may result. The relief of pain is usually immediate. Rarely is it necessary to anesthetize through the tenth interspace.

RESULTS

Fourteen patients suspected of having acute cholecystitis were treated with procaine blocks (see table). Of these, 10 had immediate and complete relief of pain lasting from 24 hours to several weeks.

At operation from one to two days after the injection six of these patients were found to have subsiding acute cholecystitis. One patient who had undergone

8. Davis, L.; Pollock, L. J., and Stone, T. T.: Visceral Pain, Surg., Gynec. & Obst. **55**: 418-427, 1932.

9. Craig, W. McK.: Surgical Approach to and Resection of the Splanchnic Nerves for Relief of Hypertension and Abdominal Pain, West. J. Surg. **42**:146-152, 1934.

10. Mandl, F.: Paravertebral Block, New York, Grune & Stratton, 1947.

11. Labat, G.: Regional Anesthesia, Philadelphia, W. B. Saunders Company, 1924.

cholecystectomy in another hospital several years before was found to have a long cystic duct remnant with surrounding scar tissue enmeshing sympathetic nerve fibers. One patient who had a long history of pyloric ulcer was found to have a normal gallbladder but an inflammatory process as a result of the ulcer in the region of the hepatic plexuses. One patient with pain and jaundice who had immediate relief from pain and rapid subsidence of the jaundice, at operation presented a normal gallbladder but demonstrated severe hepatic degeneration with cholangitis. The jaundice was interpreted as due to reflex spasm of the sphincteric mechanism of the common bile duct. In one patient who received relief the abdomen was not explored because of severe obesity (335 pounds [152 Kg.]), surgical intervention being now safely deferred until the patient could lose considerable weight.

Of the four patients who received no relief, one had multiple liver abscesses associated with typhoid with diaphragmatic and parietal wall involvement, one had a previously ruptured gallbladder with subphrenic abscess and two were not subjected to operation, a diagnosis of psychoneurosis being established after further study.

The efficacy of sympathetic block at this level in relieving the pain and aiding in subsidence of the acute cholecystic obstruction and its failure in other situations were most dramatic.

SUMMARY

In patients with early acute cholecystitis blocking of the right thoracic sympathetic trunk at the level of the eighth and ninth ganglions produces immediate relief of pain. The failure of the pain to return in most instances and the rapid subsidence of the obstructive process suggests that motor fibers have also been inhibited. In those instances in which the diaphragmatic or parietal peritoneum has been involved there has been but little relief of pain. The procedure has also served as a method of differentiating biliary tract pain of organic origin from that seen in psychoneuroses.

DISCUSSION

DR. NATHAN A. WOMACK, Iowa City: There is really not much to add to what Dr. Eastwood has said. Ordinarily one would be somewhat apologetic in presenting such a small number of cases, but the dramatic results were such that we think it is justified.

These patients, within the course of 15 or 20 seconds, are changed from acutely suffering, perspiring persons to perfectly normal, happy ones. We proposed this treatment in the beginning, in our own minds, as a method of relief of pain for a few brief hours. As was shown last year so well by Dr. Curreri and Dr. Gale, in experimental animals and clinically, the pharmacological substances that are used to relieve biliary spasm have not been too effective, and therefore often we are forced to use narcotics which increase spasm in order to relieve pain. Thus we worsen the inflammatory process.

Much to our satisfaction, there was not only relief from pain but obvious relief of spasm, as was shown in two patients with jaundice, which disappeared rapidly, and also by the fact that in only one patient was it necessary to give another injection, and that 48 hours later.

The longest duration before nerve block of any of these attacks, as I recall it, was about 48 hours. Most of them were about 18 to 24 hours in duration. We operated within 24 to 48 hours after the patient received the block in order to demonstrate, if we possibly could, evidence of acute cholecystitis; in every instance in which we found acute cholecystitis we found it subsiding. The edema was disappearing. Often the gallbladder would be wrinkled and still have fibrin around its base.

For those who do not like to operate on patients with acute cholecystitis, we offer this as a method of converting the condition into chronic cholecystitis.

Case Reports

SPLENECTOMY AND CESAREAN SECTION IN PREGNANCY COMPLICATED BY ACUTE THROMBOCYTOPENIC PURPURA

Clinical Evidence for Hormone Control of Thrombocyte Level

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THE CONCEPT of hypersplenism can theoretically be explained on the basis of a hormone-like function, overproduction of the hormone being the cause of disease states. Proof of this mechanism is lacking, particularly since animal experimentation on the pathologic physiology of the spleen has so far been unsatisfactory. Pregnancy complicated by hypersplenism, however, provides a clinical situation that can be interpreted as a controlled experiment, with comparison of the hematological condition of the mother at the time of delivery and that of the newborn infant. If the infant is born with the same disease as the mother but recovers spontaneously after separation from the maternal circulation, it would seem possible to postulate that the etiologic factor is a chemical that can cross the placental barrier. This fact was brought to our attention by a pregnant patient who at term experienced an acute purpuric crisis. A simultaneous splenectomy and cesarean section were performed, and the infant was found to have severe thrombocytopenia. Both mother and infant recovered hematologically at the same rate. A search of the literature has revealed that in every acceptable case report of a similar instance, in which the mother at delivery had demonstrable thrombocytopenia as an expression of proved purpura, hematologic studies made on the infant revealed the presence of thrombocytopenia, with or without clinical purpura. Furthermore, the surviving infants all recovered completely after their removal from the influence of the maternal circulation. As a controlled experiment, multiple pregnancies in purpuric women, with splenectomy intervening, illustrate even better the theory of hormone-like causation of hypersplenism.

REPORT OF CASE

The patient was a 26 year old trigravida, unipara, whose last menstrual period had begun on Feb. 27, 1948. She gave a history of bruising easily all her life and had been bothered particularly by frequent epistaxis as well as menorrhagia. After an induced abortion in 1944, she bled profusely and had to be hospitalized for transfusions. She first noted the presence of purpura in April, 1947, during the eighth month of her second pregnancy. At term an abruptio placenta developed which necessitated a cesarean section. While specific information is lacking, it is reported that the infant was normal. The mother's platelet count after delivery was 35,000.

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Her present gestation had been essentially normal except for frequent epistaxis until the eighth month, when she again noted the presence of purpura. Examination in the ninth month when she was referred to this hospital revealed the purpura to be diffusely present over the body as well as on the mucous membranes of the palate and pharynx. The spleen was not palpable. The infant was considered small, but the fetal heart tones were of good quality at a rate of 140; there was no vaginal bleeding. The blood pressure was 100/64. The urinalysis gave normal results.

The hematological studies performed on the patient are noted in table 1. Her Kahn reaction was negative, and the usual chemical examinations of the blood showed it to be normal. During the acute exacerbation, the patient's platelet count was reduced, the bleeding time was prolonged, clotting time and prothrombin times were normal, clot retraction was delayed, and the tourniquet test gave a positive reaction. The patient had no signs of toxemia and gave no history of ingestion or of exposure to such agents as might possibly give rise to a symptomatic type of thrombocytopenia. In addition, bone marrow studies revealed a hyperplastic state with many megakaryocytes and without actual evidence of platelet formation, a finding characteristic in essential thrombocytopenic purpura.

TABLE 1.—*Mother Laboratory Data*

	Hemoglobin, Gm.	Hematocrit, %	Red Blood Cell Count	White Blood Cell Count	Platelets	Bleeding Time (Duke's Method)	Clotting Time (Howell Method)	Clot Retraction
Mother								
5/ /47	....	..	.....	Increased	35,000	..	..	..
7/20/48	....	..	3,320,000	10,300	46,480	..	..	..
11/27/48	10.5	41	4,700,000	8,600	0	18	6	None in 24 hr.
12/ 7/48	....	33	3,170,000	.....	2,900	..	..	..
12/ 8/48	....	36	2,700,000	.....	2,600	..	..	..
Operation	....	..	.....	.....	.....	..	..	..
12/10/48	....	27.5	2,800,000	.....	62,000	1	3½	..
12/13/48	....	40	4,200,000	.....	218,000	..	..	..
2/ 1/49	14.5	49	5,000,000	8,600	80,000	..	..	..
5/24/49	13.5	42	4,500,000	6,600	65,000	..	..	..
12/20/49	13.9	42	4,850,000	7,850	223,000	7	..	..
1/16/51	11.8	39	4,200,000	10,100	90,000	..	..	..
Infant								
Birth	....	..	.....	.....	About 50,000	..	2 min.	..
4 wk.	....	..	.....	.....	90,000	..	..	..
1 yr.	....	..	3,850,000	9,500	950,000	Normal	..	..
2 yr.	8.4	..	4,900,000	5,700	315,000	..	..	..

On the eighth hospital day, two days past the expected date of confinement, severe epistaxis recurred, accompanied with gross hematuria. The platelet count at this time remained less than 3,000. Transfusions yielded only brief remission of the bleeding. By midnight the patient presented the picture of acute thrombocytopenic crisis with generalized purpura, hematuria, and bleeding from the nose, mouth, and stomach. The onset of labor at this time would probably precipitate a hemorrhage which would be fatal both for the mother and for the infant. In view of the previous history of abruptio placenta and cesarean section, the department of obstetrics believed that only by performing a cesarean section was there a significant chance of obtaining a live infant. On the other hand, the consultants in surgery and hematology were convinced that unless splenectomy was performed the bleeding accompanying a cesarean section would be so profuse that the mother would likely die. The one logical approach to the problem of treatment of the thrombocytopenic crisis at term, therefore, was to do a simultaneous splenectomy and cesarean section.

The patient was taken to the operating room, where 1,000 cc. of fresh whole blood was given immediately before operation. A high left paramedian incision was elected, which, while obviously not ideal, had the advantage of allowing a classical cesarean section through a small extension of the same incision. When the peritoneal cavity was opened, it was found that the spleen had been displaced upward and posteriorly by the enlarged uterus and could not even

be visualized. Modification of the incision, possibly by a costal margin-splitting procedure, obviously not only increased the risk for the mother but also prolonged the time before cesarean section could be performed. A decision was made to isolate the splenic artery by palpation and to occlude it with a long hemostat, thus at least interrupting the blood supply to the spleen. When this maneuver had been accomplished, 12 minutes were allowed to elapse while 1,500 cc. of blood was given through three previously placed 15 gage needles. It was encouraging to note that at the end of the 12 minutes the constant oozing from the wound margins seemed to be abating. The obstetrical team then extended the incision and performed a high classical cesarean section, delivering a living, normal-appearing male infant who weighed 3,060 gm. It should be noted that the obstetrician felt that the bleeding associated with the cesarean section was practically within normal limits. After closure of the uterus and with the obviously improved exposure, splenectomy was easily performed. A rapid but thorough attempt was made to detect any accessory splenic tissue, but none was found and the wound was closed in a routine fashion. The patient received an additional 1,000 cc. of blood during the latter part of the operation.

Postoperatively the patient had mild tachycardia. The hematocrit value was found to be only 27.5%, and we had obviously underestimated the extent of her anemia. During the course of the next three days, the hemoglobin and hematocrit values were restored to normal and tachycardia ceased. The patient was discharged with the infant on the 11th postoperative day.

After splenectomy the platelet count rapidly rose toward normal; it was 62,000 by the first postoperative day, with a nomal bleeding time. A smear of the infant's blood immediately after delivery revealed a marked reduction in platelets, estimated at less than 50,000. Four weeks later at the time of circumcision the count was still only 90,000. The counts of the mother and infant have been checked at various intervals. The infant is normal at the present time. The mother has reverted to a relative thrombocytopenia which has persisted. The child born one and one-half years previously has recently been examined and has a completely normal blood count.

Comment.—A widely held theory of the etiology of essential thrombocytopenic purpura assumes that some substance is manufactured by the spleen which inhibits the formation of the platelets in the bone marrow. This, according to Limarzi,[1] is manifest through an inhibition of platelet formation from the megakaryocytes. The marrow may be hyperplastic with many of these cells present, but some influence prevents the final maturation and the production of platelets.

For purposes of this study we have collected a series of cases from the literature in which patients had true thrombocytopenic purpura or, with an accurate history of the disease, maintained a thrombocytopenia which persisted during pregnancy following splenectomy.[2] Sufficient factual information was not presented in some

1. Limarzi, L. R.: M. Clin. North America **28**:153, 1944.

2. Bernstein, P.; Newman, A. B., and Hetzig, W. M.: Am. J. Obst. & Gynec. **38**:323, 1939. Burnett, C. W. F., and Klass, I.: J. Obst. & Gynaec. Brit. Emp. **50**:393, 1943. Davidson, L. T.: Am. J. Dis. Child. **54**:1324 (Dec.) 1937. Grossman, S.: Splenectomy in Pregnancy Complicated by Thrombocytopenia Purpura Hemorrhagica, J. A. M. A. **125**:82 (May 6) 1944. Hottenstein, H. W., and Klingman, W. O.: Am. J. Obst. & Gynec. **13**:375, 1927. McAlenney, P. F., and Kirstan, J. J.: Am. J. Dis. Child. **78**:401 (Sept.) 1949. Phython, D., and Lartz, R. E.: Am. J. Obst. & Gynec. **45**:715, 1943. Polowe, D.: Splenectomy in Pregnancy Complicated by Thrombocytopenic Purpura Hemorrhagica: Report of a Successful Case, with Review of Literature, J. A. M. A. **124**:771 (March 18) 1944. Siegler, S. L.: M. Rec. **139**:189, 1934. Urbanski, A. X., and Hunter, C. I.: Thrombopenic Purpura Complicating Pregnancy: Treatment by Splenectomy Resulting in Clinical Cure and Followed by 3 Full Term Pregnancies, J. A. M. A. **120**:754 (Nov. 7) 1942. Greenwald, H. M., and Sherman, I.: Am. J. Dis. Child. **38**:1245 (Dec.) 1929. Mosher, G. C.: Surg., Gynec. & Obst. **36**:502, 1923. Sanford, H. N.; Leslie, E. I., and Crane, M. M.: Am. J. Dis. Child. **51**:1114 (May) 1936. Schefrin, A. E., and Schechtman, A.: Am. J. Dis. Child. **70**:29 (July) 1945.

of the series previously collected,[3] and many of these cases therefore could not be included in this analysis. Nine additional reports from the more recent literature [4] have been gathered in which adequate and pertinent information is presented.

There are 28 cases, including our own, in this series (table 2). In 17 patients the delivery was preceded by a splenectomy or simultaneous splenectomy and cesarean section was performed. In 12 instances, delivery occurred without previous splenectomy. One patient is included in both groups since there is detailed information presented concerning pregnancies both before and after splenectomy.

Splenectomy was performed prior to gestation in seven instances (table 3). All patients give an accurate history of essential thrombocytopenic purpura, and, though clinically normal in that at most they demonstrated only an occasional purpuric spot, they all had evidence of thrombocytopenia at the time of delivery. Seven of the patients underwent splenectomy during the course of the pregnancy, while in three the splenectomy was performed at term. The latter group includes two patients in whom simultaneous splenectomy and cesarean section was per-

TABLE 2.—*Essential Thrombocytopenic Purpura in Pregnancy*

Total cases	28 *
Cases with splenectomy	17
Cases without splenectomy	12

* One patient was presented on whom adequate studies were made during a pregnancy both before and after splenectomy.

TABLE 3.—*Relationship of Splenectomy and Pregnancy*

Splenectomy performed before pregnancy	7
Splenectomy during pregnancy	7
Splenectomy at term	3

formed. The incidence of persisting thrombocytopenia in seven of 17 patients seems rather high when one considers the generally accepted efficacy of splenectomy in the treatment of essential thrombocytopenic purpura. It should be remembered that all seven of these patients were considered clinically cured of their disease. However, both Limarzi and Minot believe that the incidence of a persisting thrombocytopenia following splenectomy may be at least 20%.

If the factor responsible for the thrombocytopenia is a hormone-like substance, it is possible that it could cross the placental membrane and produce subsequently

3. De Saussure, H. W., and Townsend, E. B.: Am. J. Obst. & Gynec. **29**:597, 1935. Finn, W. F.: Am. J. Obst. & Gynec. **48**:497, 1944. Rushmore, S.: Am. J. Obst. & Gynec. **10**:553, 1925.

4. (*a*) Arrowsmith, W. R.; Tyrone, C., and Lyons, C.: J. Lab. & Clin. Med. **34**:1580, 1949. (*b*) Barnes, A. C., and Doan, C. A.: Am. J. Obst. & Gynec. **55**:864, 1948. (*c*) Dinsmore, R. S., and Dutlinger, R. P.: Cleveland Clin. Quart. **13**:128, 1946. (*d*) Epstein, R. D.; Lozner, E. L.; Cobbey, T. S., Jr., and Davidson, C. S.: Am. J. Med. **9**:44, 1950. (*e*) Morrison, M., and Sanwick, A. A.: Am. J. Dis. Child. **70**:115 (Aug.) 1945. (*f*) Norland, M.; Ylnisaker, R. S.; Larson, P., and Reiff, R.: Minnesota Med. **29**:166, 1946. (*g*) Patterson, W. B.: Thrombopenic Purpura in Pregnancy and in the Newborn, J. A. M. A. **130**:700 (March 16) 1946. (*h*) Stroebel, C. F.; Campbell, D. C., and Hagedorn, A. B.: M. Clin. North America **33**:1027, 1949. (*i*) Talmadge, J., and Berman, B.: J. Pediat. **30**:691, 1947.

detectable effects on the infant in utero. If such were the case, infants born to mothers with thrombocytopenia should similarly show evidence of this condition.

Falls [5] has shown that the factor producing eosinophilia in pregnant women with asthma passes the placental barrier and produces eosinophilia in fetal blood. He has also shown that bacteriolysins and agglutinins for the organism producing pyelitis in the mother appear in fetal blood.

Twelve patients were delivered without splenectomy and thus had thrombocytopenia at term. In the nine instances in which platelet counts were performed

TABLE 4.—*Thrombocyte Level in Infants of Mothers on Whom Splenectomy Was Not Performed* *

Maternal thrombocytopenia at delivery	12	
Infants with thrombocytopenia	9	
Infants without thrombocytopenia	1	
Infants without specific platelet counts (considered normal)	4	
Stillborn infants (no observations)	1	
Total no. of infants	15	
Total no. of maternal observations	12	

* One patient was studied during three pregnancies.

TABLE 5.—*Thrombocyte Level in Infants of Mothers Who Underwent Splenectomy* *

Maternal thrombocytopenia early; normal at term	7	
Infants with thrombocytopenia	0	
Infants without thrombocytopenia	3	
Infants without specific platelet counts (considered normal)	3	
Stillborn infants (no observations)	1	
Infants	7	
Maternal observations		7
Maternal thrombocytopenia at delivery	10	
Infants with thrombocytopenia	13	
Infants without thrombocytopenia	0	
Infants without specific platelet counts (considered normal)	1	
Stillborn infants	1	
Infants	15	
Maternal observations		10
Total no. of infants	22	
Total no. of maternal observations		17

* One patient had two pregnancies, and two others had three; hence there are 22 infants and 17 patients.

on these infants, thrombocytopenia existed. One infant was reported to be born without thrombocytopenia.[4d] The platelet count on this infant was not determined until the fourth day, at which time it was 188,000. By the seventh day it was 304,000. This rising count is suggestive, at least, of a release from a depressing influence. In four instances the infants were considered "normal," but specific platelet counts were not performed. One infant was stillborn.

The patients who underwent splenectomy can be divided into two groups (table 5). In one the thrombocytopenia was present early in the period of gestation, but the platelet count was normal at term; in the other the thrombocytopenia persisted at the time of delivery. In the former group, splenectomy performed

5. Falls, F. H.: A Contribution to the Study of Pyelitis in Pregnancy, J. A. M. A. **81:** 1590 (Nov. 10) 1923.

early in pregnancy relieved the existing thrombocytopenia. In the latter group, thrombocytopenia persisted in spite of splenectomy performed prior to or during gestation.

The seven patients who had thrombocytopenia early but were normal at term produced no infants with thrombocytopenia. Platelet counts generally were not recorded, but the infants were reported to be normal. One infant was stillborn.

There were 10 splenectomized patients who had thrombocytopenia at the time of delivery. This group included the seven patients who had persisting thrombocytopenia following previous splenectomy as well as the three patients in whom splenectomy was performed at term. Thrombocytopenic counts are recorded for 13 infants born to these 10 mothers. In one instance no specific platelet count was presented, and one infant was stillborn. One of the patients in this category had two pregnancies and two others had three, so that there are 15 infants included in this particular group.

COLLECTED CASE REPORTS

The following summaries of cases reported elsewhere are illustrative of the types included in this series:

CASE 1.[4]—The patient, a 22 year old primigravida, was known to have had purpuric manifestations since the age of 4. Menorrhagia had been present since the onset of menses at the age of 13. Her course during pregnancy was uncomplicated except for the presence of purpura. A platelet count was recorded of 62,000; the bleeding time was prolonged and the clotting time normal.

Delivery occurred spontaneously and was uneventful except for rather brisk bleeding from a tear in the vaginal wall which required packing of the vagina as well as suture repair to control. No significant uterine bleeding was noted, however. Five days post partum the platelet count was 60,000; there was no clot retraction in 24 hours. At 37 days post partum the platelet count was still only 36,300 though the bleeding time was normal.

The infant weighed 7 lb. 4 oz. (3.3 kg.); one small purpuric spot was noted on the forearm. By 72 hours after birth, however, frank blood was noted in the stools. The platelet count was 18,570. The infant improved, and by the 75th day the platelet count was 175,000. There was no evidence of purpura at that time.

This case illustrates a situation in which the mother had thrombocytopenia which persisted to the time of delivery. The infant born also had thrombocytopenia, but once free of the maternal influence a normal number of platelets gradually developed.

CASE 2.[6]—This patient had a diagnosis of essential thrombocytopenic purpura established when she was 14 years old, in 1926. A splenectomy was performed at that time. Twelve years later, at the age of 26, the patient became pregnant. The platelet count when she was first seen was only 70,000 though the bleeding time was normal. Her period of gestation was uneventful and the only abnormalities were the persistent thrombocytopenia and no evidence of clot retraction. The infant, when delivered, had many purpuric spots; the platelet count was 80,000. The condition progressed, and the baby died from an intracranial hemorrhage three days after birth.

Two years later the patient again became pregnant. Thrombocytopenia (platelet count of 62,000) and the absence of clot retraction persisted. At birth the second infant had only a few purpuric spots; the platelet count was 90,000 and the bleeding time 11 minutes. However, the hemorrhagic spots became more pronounced, and the course was rapidly downhill; the infant died 24 hours after birth.

In this patient, the thrombocytopenia persisted in spite of a splenectomy. Both infants had thrombocytopenic purpura which had a fatal outcome.

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6. Whitney, L. H., and Barritt, A. S., Jr.: Am. J. Dis. Child. **64**:705 (Oct.) 1942.

CASE 3.[4b]—The patient, a 21 year old white woman, was first seen when she was seven months pregnant with her first child. She gave a history of bruising easily and of noting the presence of purpuric spots. While under observation her platelet count varied from 6,000 to 12,000, and examination of a bone marrow smear revealed a hyperplastic state. A splenectomy was performed. A few hours postoperatively the platelet count was 39,600. By the sixth day it had risen to 497,700, and it remained within normal limits. At term, labor began spontaneously, and a normal infant was delivered without evidence of purpura or hemorrhagic tendency.

This patient had the characteristic picture of essential thrombocytopenic purpura which responded to splenectomy during pregnancy. At term, her platelet count was normal. Likewise, the infant's counts were normal, and no evidence of purpura was noted.

Comment.—The idea of a hormone-like substance mediating the factor responsible for thrombocytopenia in essential thrombocytopenic purpura is not unique and, as a matter of fact, was first mentioned by Liebling in 1926.[7] Troland[8] in 1938 actually produced acetone extracts of splenic tissue from patients with essential thrombocytopenic purpura which, when injected into rabbits, produced a marked drop in platelets. However, the work has not been confirmed. Specific observations and correlation of clinical material have not been presented previously. None of the patients in this series who had a normal thrombocyte level at the time of delivery produced infants with thrombocytopenia even though there was an accurate history of essential thrombocytopenic purpura. Conversely, in each of the cases in which the infant's platelet count was recorded and the mother had thrombocytopenia at the time of delivery, thrombocytopenia was noted in the infant, with the exception of the case in which there was a low and rising platelet count on the fourth day. It should, of course, be mentioned that in some instances specific platelet counts were not determined on infants born to mothers with thrombocytopenia; all these infants were considered "normal." The infant in our case also was considered normal but had definite thrombocytopenia as determined by a specific count. In view of the fact that all the infants in this group on whom platelet counts were determined (even the two infants considered normal) had thrombocytopenia, it is possible that the others also carried this abnormality.

We believe that the clinical evidence presented strongly suggests the presence of a hormone-like substance in the circulation of pregnant patients with essential thrombocytopenia. That this substance crosses the placental membrane to act on the fetus in utero is evident from the consistent thrombocytopenia present in the infants in whom thrombocyte levels were determined. That the substance is elaborated not always by the spleen but possibly also by extrasplenic reticuloendothelial tissue is suggested by the occurrence of transmittible thrombocytopenia after splenectomy when adequate search has been made for accessory splenic tissue.

SUMMARY

A case of an acute exacerbation of essential thrombocytopenic purpura in a pregnant patient at term is presented. The pertinent findings in 28 cases of essential thrombocytopenia in pregnancy are reviewed. Clinical evidence is presented which suggests that a hormone-like substance mediates the factor responsible for the thrombocyte level in patients with essential thrombocytopenic purpura.

7. Liebling, P.: Am. J. Obst. & Gynec. **11**:847, 1926.

8. Troland, C. E., and Lee, F. C.: Thrombocytopen: Substance in Extract from Spleen of Patients with Idiopathic Thrombocytopenic Purpura That Reduces Number of Blood Platelets, J. A. M. A. **111**:221 (July 16) 1938.

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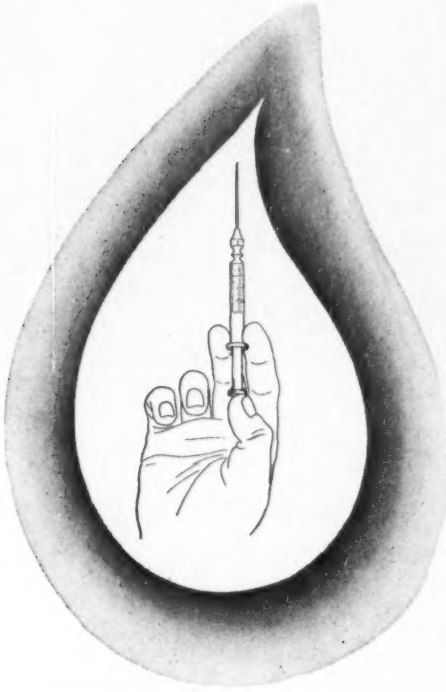

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